Outpatient management of preeclampsia: How long?

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Hypertension in pregnancy and preeclampsia are among the major causes of hospital admission. Mother safety is the first issue to consider when facing the disease but a comprehensive management should also take into account when admission should be warranted and when, conversely, outpatient treatment is feasible.

A recent meta-analysis supports outpatient management for gestational hypertension and mild preeclampsia and we developed a specific protocol to follow up such patients in a dedicated Clinic admitting into hospital only severe preeclamptic, on time to stabilize maternal conditions and proceed with expedite delivery.

The first step is to correctly select the patients and assign them to the hypertensive subset according to the severity through careful medical history, blood tests, blood pressure recording, fetal growth assessment.

Outpatient management included regular visits at our Clinic where the patient underwent clinical evaluation; at the end of every visit, the Doctor decided to keep the woman as outpatient or proceed with hospitalization.

In our four-year experience 13.5% patients required immediate hospitalization (IH group) and were promptly delivered, 35.1% women eligible for outpatient follow-up subsequently worsened and required admission (OUT-H group), and 51.4% were followed-up as outpatient until delivery (OUT group).

More specifically, 75% of the women who presented with Gestational Hypertension (GH) remained in the OUT group, 25% shifted in the OUT-H; 22.2% of women with GH associated with intrauterine fetal growth restriction (GH+IUGR) remained in the OUT group, 55.6% were in the OUT-H, 22.2% required IH; 60% of women with mild Preeclampsia (mild PE) remained in the OUT group, 40% shifted to the OUT-HA group.

Our experience shows that an outpatient management for hypertensive disorders in pregnancy is feasible with safety and reduced costs, provided that careful selection is made at every visit.
Expectant management of severe preeclampsia

Sao Paulo, Brazil

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Objective: The aim of the present study was to verify the maternal morbidity and perinatal outcome associated with expectant management in pregnancies complicated by severe preeclampsia.

Study Design: prospective analysis of maternal and perinatal morbidity of 169 singleton pregnancies complicated by severe preeclampsia (expectantly managed) was conducted at the Hospital das Clínicas da FMUSP, from January 2004 to December 2007. After hospital admission, maternal and fetal surveillances (cardiotocography, biophysical profile score (BPS), amniotic fluid index and Dopplervelocimetry) were performed. Delivery was performed if any of these maternal or fetal condition were present: imminent eclampsia, eclampsia, HELLP syndrome, hypertension unresponsive to three different drugs in maximal doses, renal insufficiency, abruptio placentae, labor or rupture of membranes, gestational age ≥37 weeks and abnormalities in the fetal well-being tests. The administration of antenatal corticosteroids followed by caesarean section after 48h was indicated when Ductus venosus pulsatility index was between 1.0 and 1.5 or AFI ≤5.0 and gestational age <34 weeks.

Results: The gestational age at the time of admission was 25 to 29 (55 cases), 30 to 33 (56 cases), and 34 to 36 (58 cases) week gestation. The mean value of pregnancy prolongation was 14.7 days (SD=11.8 days). Pregnancy prolongation was ≥7 days for 73.4%, ≥14 days for 45.6%, ≥21 days for 24.9%, and ≥28 days for 11.8%. Delivery was performed due to gestational age ≥37 weeks (51 cases, 30.2%) fetal distress (67 cases, 36.6%), imminent eclampsia (8 cases, 4.7%), deterioration of hypertension (4 cases, 2.4%), worsening renal insufficiency (2 cases, 1.2%), abruptio placentae (2 cases, 1.2%), and eclampsia (1 case, 0.6%). There was no maternal death.

Conclusion: Expectant management of severe preeclampsia could be performed in the tertiary perinatal center as soon as proper selection of patients and close monitoring of mother and fetus are performed.
Background: Several trials compared glibenclamide to insulin for the treatment of gestational diabetes mellitus (GDM), and demonstrate excellent results (1, 2, 3). Recently a systematic review (4), selected four randomized prospective trials with anti diabetic agents (glibenclamide, acarbose and metformin). The authors conducted a meta-analysis for some variables with glibenclamide and a sensitive analysis. The benefits of these drugs compared to insulin for the treatment of GDM without perinatal risks are demonstrated.

At first we conducted a trial comparing glibenclamide to insulin and we demonstrate maternal glycemic control equal in both groups and safety of the drug for the newborns (1).

Since 2008 we are conducted another trial comparing glibenclamide and metformin.

Design: Multicentric randomized, open trial is been conducted on several services of Joinville-Santa Catarina, since 2008. The pregnant women with gestational diabetes (diagnosis using WHO criteria) were randomized for the use of glibenclamide or metformin. These gestational diabetics were between 13th and 33rd weeks of gestation, a single pregnancy and no other complicated pathologies. When the maximum dose of glibenclamide (20mg) or metformin (2500mg) are reached, these drugs are replaced for insulin, in order to achieve the best maternal glycemic control during pregnancy. The analysis included: maternal glycemic control during pregnancy (fasting and pos prandial glycemic levels); birth weights of the newborns and neonatal hypoglycemia doing periferic capillar glycemia (PCG) at 1, 3 and 6 hours after birth.

Preliminary Results: Until now 90 patients were included for the study, and of these six were excluded.

37 gestational diabetics had delivery her babies, 19 in the group of glibenclamide and 18 on the group of metformin. No differences were found in both groups related to age of the patients, body mass index (BMI) and gain of weight during pregnancy.

Six (16 2%) patients need to change therapy for insulin in order to have good glycemic control: 3 in each group. No differences in the fetuses weights (p=0.72); 6 (16.2%) were large for gestational age (LGA), 4 in the group of glibenclamide and 2 in the metformin.

No difference in the PCG of the newborns at 1st hour (p=0.33) and 6th hour (p=0.36), but at 3rd hour the PCG were less (p=0.04) in the group of glibenclamide. Hypoglycaemia of the neonate occurred in 3 (8.1) cases in the group of glibenclamide (normal level>39mg/dl).

Conclusion: At the present moment both glibenclamide and metformin were efficient for maternal glycemic control and safety with few cases 3 (8.1) of LGA and the same for hypoglycaemic babies.

Reference List
Reports have shown that even in western countries, spontaneous abortions may be as high as 17%, the stillbirth rate to be 5-times greater, congenital malformations to range from 4 to 10 times the usual rate, perinatal mortality to be 5-fold, neonatal mortality 15 times greater, and that infant mortality might be trebled as the Result of diabetic pregnancies. These poor Results have also been reported for type 2 diabetics and range from congenital malformations 11 times greater, a 2-fold risk of stillbirth, perinatal mortality 2.5 times higher, risk of neonatal deaths 3.5 times greater and a 6-fold risk of death in the first year of life. Gestational diabetes mellitus (GDM) usually develops in the second half of pregnancy. Congenital malformations aside, the whole spectrum of peri(neo)natal problems overlap those of pre-GDM and contribute to the high maternal-fetal and neonatal morbidities.
Neonatal complications of the IDM - stillbirth and birth asphyxia, congenital malformations, macrosomia and birth injury, jaundice, polycythaemia/hyperviscosity syndrome, hypoglycaemia, hypocalcaemia, RDS, hypertrophic cardiomyopathy, hypoplastic left colon syndrome - are now quite well managed with intensive neonatal care.
The long-term outcome, on the other hand, poses several questions. A major issue is whether some adult diseases of metabolic and vascular disorders may have had a fetal origin.
Priority should focus on intensive prenatal care for diabetic women and the identification of women for the development of GDM and, once diagnosed, placing them on a strict glycemic control throughout pregnancy. The cost efficiency of screening all women for GDM is often discussed and likewise, whether many of these women are over-treated unnecessarily. Argument, however, should concentrate not just on the immediate effects of GDM but on the long-term consequences for both the mother and her offspring.
The role of fetal echocardiography in diabetic pregnancies

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Gestational diabetes mellitus is a major health problem, concerning the whole world with more than 500,000 children born yearly from mothers with diabetes. In the US 5% of the new born children requiring intensive therapy in the post partum period belong to this collective. Gestational diabetes has serious, long-term consequences for both mother and baby, including a predisposition to obesity, metabolic syndrome, and diabetes later in life. The incidence of fetal malformations are also increased in these new born patients, reaching 5 to 10%. Perinatal mortality is caused in 30-50% of the cases due to congenital malformations. The most common malformations implies the CNS, being 10 times increased, cardiac malformations being 5 time increased, and the most common is sacral agenesis or the caudal dysplasia. Hypertrophic cardiopathy represents the most common cardiac malformation seen in fetuses from mother with gestational diabetes. The ultrasound can detect the septal and ventricular hypertrophy, allowing the early treatment. The septal defects can also be detected using the ultrasound and the four-chamber view. The diagnosis of transposition of great vessels remains the one of the most difficult diagnosis, requiring experience and technical skills. In this case the right section is the one along the axis of the left heart. Early detection and intervention can greatly improve outcome for women with this condition and their babies, the second trimester ultrasound screening plays a very important role in evaluating the fetal outcome in diabetic pregnancy.
Ultrasound has truly revolutionized the practice of obstetrics. It is hard to imagine doing antenatal care without U/S. However its ultimate usefulness is highly dependent on the personal experience and his capabilities in the interpretation of U/S images being obtained and also on the evaluating the data obtained.

With more and more sophisticated and advanced machines, the level of fetal details obtained are much enhanced.

Initial studies conducted to study some bizarre U/S findings in the fetus or surrounding in mid trimester pregnancy scan were almost all of them are retrospective case series.

These initial studies drew some conclusions regarding these findings specially when seen in pregnant women with a high risk probability of having an abnormal child and sometimes the clinical decision of fetal intervention or termination of pregnancy has been taken based solely on these studies or observations.

As with advancement of research evidence based approach is suggested for most issues related to medicine.

With second approach by to theses conflicting sign by well designed studies we could extract some sort of protocol for management in theses cases.

My article tries to shed some light on some of theses controversial U/S like: Echogenic bowel-Club foot- renal pylectasis –intracardiac foci – choroid plexus cyst – polydactyly – single umbilical artery, trying to present the most available data to suit out an evidence based approach to their management and to provide the clinician with all the data that enables him to properly council the parents and eliminates the confusion created by the mere detection of theses findings.
Prenatal diagnosis of fetal limb defects using 3D/4D ultrasound

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Anomalies of the limbs occur in approximately 2.2% of all newborns. There may be general abnormalities of bone and cartilage growth, or changes may be confined to individual bones or limb segments.

In contrast to 2D sonography 3D ultrasound offers the ability to demonstrate the fetal limbs in four different display modes: multiplanar, tomographic, surface and transparent modes. With 4D ultrasound the limb movements can be visualized three-dimensionally in real time. 3D/4D ultrasound technology gives us the capability to store not just two-dimensional images but complete volumes.

In clinical use, the different 3D and 4D views of the fetus offer the physician several advantages in the detection or exclusion of fetal limb abnormalities. The interactive display is particularly useful to identify general skeletal anomalies or isolated abnormalities of limb segments.

Since in 3D ultrasound the examination is not performed on a moving fetus but on a digitally stored limb that can be freely rotated in space, it is easy to recognize abnormal body proportions in skeletal dysplasias and angular deformities such as club foot or club hand. The same applies to detailed examinations of the hand and foot. The 3D surface analysis can clearly reveal the absence of a finger or the presence of an extra digit. The transparent display reveals ossification defects and abnormal curvature or fractures of the limb bones.

Comparing 2D and 3D ultrasound Results in 124 fetuses with limb anomalies, 3D ultrasound provided diagnostic advantage in 90.3% of the cases.

Summary: 3D/4D ultrasound does not only enable a precise demonstration of malformations of the fetal limbs, but can also provide more convincing evidence of normal fetal limb structures than 2D ultrasound.
Prenatal diagnosis of fetal tumors and cysts

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Objective: To establish sonographic guidelines for prenatal detection of fetal tumors and cysts.
Design and methods: All cases of fetal tumors and cysts detected during the period May 1st 1995 - July 31st 2009, were analyzed. Once a fetal tumor has been detected, close surveillance by a multidisciplinary team has been conducted. Problems regarding management during pregnancy, labor and immediate postnatal life have been discussed. Management strategies included continuation of pregnancy with or without intrauterine treatment or termination of pregnancy in hopeless cases.
Results: In all cases of fetal tumors, sonographic markers and signs for prenatal diagnosis were present. Fetal tumors were found in the cranium, face and neck, thorax, abdomen, musculoskeletal system, cardiovascular system and in various internal organs. Sonographic criteria have been developed and classification by site has been formulated as follows:
- Head and brain
- Face and neck -
- Thorax (including heart)
- Abdomen and retroperitoneum
- Other:
  - Extremities
  - Sacrococcygeal region
  - Genitalia
- Skin
Conclusions: Fetal tumors are rare, but are associated with serious illness or even death in the fetal or neonatal period. Therefore, the prenatal diagnosis of fetal tumors has significant implications on the well-being of both mother and fetus, as well as on perinatal and neonatal outcome.
The fetal face – 3D/4D ultrasonography

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Most of the genetical and syndromical diseases of the human have a strong impact over the facial features, a fact that may be detected even from prenatal life, starting from a very early age. In most of the cases this is done by the use of conventional 2D ultrasound, which, in expert hands, may offer good anatomical details starting from the end of the first trimester in a number of cases and from mid second trimester in most of the patients, as part of the routine second trimester anomaly scan. Without the purpose of making a statistically significant study, we analyzed different fetal pathologies by comparing the two dimensional image and the data obtained by 3D/4D ultrasound. Three-dimensional acquisition of the fetal face offers a good panoramic image of the face, including anatomical details that are not readily available in two-dimensional ultrasound. The examination time is shortened and in most of the cases the pathological aspects are obvious even for less trained sonographers and, also, for the parents. The best diagnostic images are obtained after the first trimester, and the 3D/4D techniques are especially useful in evaluating the fetal profile, size and position of the mandible, angle of the palpebral fissure, morphology and size of the ear. The motion image is particularly important in demonstrating fetal behavior, mimics and active movements, presumably related to normal neurological development. In conclusion, apart from its “commercial” aspects, parental – fetal bonding, 3D/4D ultrasound may add important details to diagnostic, especially in doubtful cases.
Multifetal embryo reduction in quadruplets and more

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Assisted reproductive technology (ART) has dramatically increased multifetal pregnancies and therefore the possibility of embryo-reduction (ER) in order to reduce premature deliveries, perinatal/neonatal mortality and morbidity and maternal complications. Even if new ART approaches tend to reduce the number of in utero embryo transfer, intrauterine insemination (IUI) or drugs stimulation and timed vaginal intercourse (TVI) cannot prevent multifetal pregnancies.

Since many years multifetal embryo-reduction is performed to reduce the number of fetuses (usually from 3 to 2 fetuses) and the most common procedure is via a transabdominal route by injection of 0.5-1ml of KCl in embryo thorax by spinal needle under continuous ultrasound monitoring, at 11-13 weeks of gestation.

In this study we describe the technique used in our department and also results and the outcomes in 25 cases of grand order multifetal pregnancies (over 3 embryos, from 4 to 9).

The protocol used in our department is based on counselling and information about risk and benefits, written consent, discussion about CVS or amniocentesis, precisely mapping of all fetuses anatomy and placentas chorionicity by ultrasound examination, fetal nuchal translucency screening before embryo reduction in order to choose which embryos to reduce and perinatal outcome.

In very high order of multiple (from 6 to 9) we usually performed embryo reduction in two session. We also discussed the results of chorionic villous sampling (CVS) before procedure or amniocentesis at 16 weeks of gestation following embryo reduction and also financial cost, ethical, psychological and legal issues.

Above all multifetal embryo reduction is recommended in high order multiples to assure good maternal and perinatal outcomes.
Doppler in abnormal pregnancy

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Transvaginal color Doppler is a rapid guide for detection of blood flow signals in the entire pregnant pelvis. Once vessels are identified by color or power Doppler ultrasound, pulsed Doppler is used to quantify the hemodynamic events. Color Doppler ultrasound is an useful tool for detection and follow up of the patients with abnormal early pregnancy, such as threatened and missed abortion. In cases complicated with subchorionic bleeding, Doppler ultrasound enables follow up of the blood flow changes occurring in spiral arteries due to mechanical compression of the near lying hematoma. In patients with incomplete abortion, two- (2D) and three dimensional (3D) color and power Doppler ultrasound allows identification of the residual products of conception. Doppler facilities can efficiently detect peritrophoblastic flow, typical for ectopic pregnancy. Patients undergoing conservative management or expectative treatment of ectopic pregnancy at different anatomic sites require careful follow up by color and/or power Doppler ultrasound. Detection of persistent color signals and low vascular impedance to blood flow indicate an active trophoblast, which requires immediate action. In patients with fetal anomalies, implementation of 2D and 3D color and power Doppler imaging permits the physician to establish the topography and origin of fetal anomalies, and provides valuable information about morphological defects of fetal circulation and umbilical cord vessels. Color and power Doppler evaluation of the patients with gestational trophoblastic disease documents the presence of enlarged spiral arteries feeding vesicular spaces with prominent arterio-venous shunting. This method can assist the sonographer in detection of recurrences of the gestational trophoblastic disease and progression to choriocarcinoma.

2D and 3D color and power Doppler ultrasound remains a subject of intense research in perinatal medicine and has become a useful tool for providing up-to-date care of the patients with pregnancy complications.
Fetal hemodynamics and umbilical cord anomalies

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Intrauterine growth restriction (IUGR) represents one of the most important challenges of perinatal medicine. IUGR is the second leading cause of perinatal morbidity and mortality. This condition caused by diverse pathologies but it is mainly related to placental insufficiency. Our study aims to investigate whether an atypical umbilical coiling pattern at prenatal sonography is associated with IUGR and adverse pregnancy outcome.

Excluding the most frequent causes of IUGR, mainly utero-placental insufficiency, we observed that the presence of hypercoiling can be associated with hemodynamic abnormalities, IUGR and oligohydramnios.

Particularly, in presence of IUGR and hypercoiling of the cord, the hemodynamic pattern was characterized by the umbilical vein pulsations and high velocity. This was evident throughout most of the hypercoiled segments of the cord, even in absence of abnormal flow in other fetal districts such as in the umbilical artery, ductus venosus, inferior vena cava and in the middle cerebral artery. This altered hemodynamic pattern was present mainly in the insertion site of the umbilical vein on the fetal abdominal wall. In this point, we observed greater umbilical vein waveform profile alterations, with umbilical vein flow velocity reaching values 2-6 times the normal values. In addition, the maximum speed of the vein appeared to be 2-3 times higher than the peak systolic velocity of the umbilical artery in the same tract of the cord.

Our study shows that the presence of hypercoiling can be associated with IUGR with unusual hemodynamic feto-maternal pattern, with an increased risk of unfavorable pregnancy outcome.
Non-invasive prenatal diagnosis of fetal chromosomal aneuploidy: State of the art

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Current methods for definitive prenatal diagnosis of chromosomal aneuploidy, such as chorionic villus sampling and amniocentesis, are invasive and associated with a risk of fetal miscarriage. In 1997, our group reported the presence of fetal DNA in maternal plasma and offered new possibilities for non-invasive prenatal diagnosis. However, fetal DNA exists as a minor fraction among a high background of maternal DNA. Hence, quantitative perturbations caused by an aneuploid chromosome in the fetal genome, e.g. chromosome 21 for Down syndrome, to the total amount of sequences from that chromosome in maternal plasma would be small. We reasoned that massively parallel genomic sequencing approaches could be applied to the non-invasive prenatal detection of aneuploidies by measuring the relative amounts of sequences from the aneuploid chromosome in maternal plasma. We used the Illumina ‘Solexa’ platform to sequence over 10 million sequence tags per maternal plasma sample. From these data, we quantified chromosome 21 sequences in first and second trimester maternal plasma samples from trisomy 21 and euploid pregnancies. Increased sequenced reads from chromosome 21 was readily identified among the trisomy 21 pregnancies. This work demonstrates the potential of massively parallel plasma DNA sequencing as a strategy for non-invasive fetal aneuploidy detection. The work also affirms the potential of quantitative sequencing by massively parallel approaches as a diagnostic tool.
New technology to make prenatal diagnosis from fetal cells and ffDNA in maternal blood

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Recent studies have demonstrated the presence of fetal cells (such as erythroblasts and stem-cells) in maternal blood and some methods have emerged for isolation of these, thus providing a promising approach for non-invasive prenatal diagnosis of genetic abnormalities. Until now, the principal approaches, in which fetal cells have been tested in non invasive prenatal diagnosis, are the detection of fetal trisomies and the determination of fetal gender by using FISH technique. Another possibility of non invasive prenatal diagnosis began in 1997, when Lo et al. showed the presence of free fetal DNA (ffDNA) in maternal plasma and serum. The studies following this discovery have proved that ffDNA is present in maternal circulation from the first weeks of gestation and it degrades in few hours after delivery; therefore it cannot interfere with prenatal diagnosis of subsequent pregnancies. Therefore ffDNA is a perfect candidate for developing new non invasive prenatal diagnosis strategies such as fetal sex determination, that Results of great importance in the management of pregnancies at risk for X-linked diseases and for the fetal RhD genotype determination in RhD negative pregnant women at risk for a RhD positive fetus. Several authors have demonstrated the possibility of detecting specific sequences for the Y chromosome and for the RhD gene in ffDNA extracted from maternal blood during gestation employing real-time PCR technique. It is possible to use different types of primers and probes specific for chromosome Y, but the most promising is the multicopy DYS14 sequence located within the TSPY gene, while for the RhD gene, located on the chromosome 1, the most promising are the Exons RhD5 e RhD7.

On the basis of this knowledge, we have been investigating the sensitivity and specificity of employing real-time PCR technique and ffDNA for non-invasive prenatal prediction of fetal gender. Moreover we have been developing a testing for the determination of the fetal RhD status by employing Real Time-PCR and the specific sequences, the Exons RhD5/RhD7. For the diagnosis of fetal gender, we have analyzed 350 samples from healthy pregnant women at 9-12 weeks gestation by using an original ffDNA-based DYS14 protocol and real-time PCR assay, to establish the sensitivity, specificity, and predictability of the testing. For the determination of fetal RhD status, we have analyzed 56 samples from RhD negative pregnant women at 9-12 weeks gestation by using a ffDNA-based Exon5/7 protocol and real-time PCR assay, to establish the sensitivity, specificity, and predictability of the testing. The data obtained by the DYS14 assay showed an efficiency in fetal gender prediction of 100%, with 100% sensitivity and 100% specificity establishing that DYS14 assay is the best approach for early fetal gender assessment because it is sensitive, accurate and efficient. The data obtained by the Exon RhD5/RhD7 assay showed an efficiency in the determining the fetal RhD status of 97% with a sensitivity of 95% and specificity of 100% in 56 cases. Moreover, we are carrying out a study on non-invasive prenatal screening test (SAFE test) which consists in a genetic analysis of fetal stem cells (CD34+) isolated from peripheral maternal blood useful to detect the majority of the fetus affected by trisomies 13, 18 and 21, which are the most frequent diseases in born alive. So far, with over 1500 assays, the test has proven to be 100% specific for all trisomies and 95% sensitive for trisomy 21, 94% for trisomy 18 and 92% for trisomy 13. This test could be an interesting approach for a future non-invasive prenatal diagnosis, safe for the fetus, available for all pregnant women and not only for those with a specific risk of getting a fetus affected by genetic abnormalities.
Fetal RHD determination in maternal plasma

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The availability of non-invasive prenatal diagnosis for the fetal RhD status (NIPD RhD) is an obvious benefit for alloimmunized pregnant women. In several recent studies fetal RHD sequences have been detected by the amplification of cell-free fetal (cff) DNA extracted from maternal plasma with real-time PCR. This diagnostic tool is now available in many laboratories around the world. Interestingly there are considerable differences when requirements for preanalytics, cff-DNA extraction, RHD exons selected, instruments and protocols for final data interpretation are compared in the published studies. Similarly differences in sensitivity and specificity can be noticed. Partners of the Special Non-Invasive Advances in Fetal and Neonatal Evaluation (SAFE) Network of Excellence funded within the European framework 6 program from 2004-2009 developed a protocol which can be used for validation of NIPD RhD assays. Additionally an external quality assurance scheme and reference material for the calibration of new assays has been established. In some countries NIPD RhD will be applied very soon in all D-negative pregnant women in order to target antenatal anti-D prophylaxis to only those women who carry a D-positive fetus. Recent developments for the use of cff-DNA controls will further reduce the number of false-negative determinations, of which a few cases have been observed in larger studies. It is necessary that patent negotiations will lead to cost-effective screening in order to abolish unnecessary administration of blood products in millions of women.
Molecular genetics of fetal chylothorax and hydrops: Significance for in utero therapy

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Fetal chylothorax is one of the very few fetal disorders that had been proved to be benefited from fetal therapy. In utero effective treatments include two mainstream modalities: thoracoamniotic shunting and antenatal pleurodesis. The speaker’s group had treated quite a few fetuses with prenatal chylothorax and probably owns the largest such series in the world. According to the previous studies from the speaker’s group as well as from elsewhere, fetuses with prenatal chylothorax can be roughly subdivided into two major subsets: one subset composed of fetuses whose pathogenesis of chylous pleural effusion to be more inflammation-mediated, which responded very well to antenatal pleurodesis. Another subset of fetuses was suspected to be genetic-related and the response to in utero therapy was very poor.

Gene loci that play important role in lymphangiogenesis, including VEGFR3, FOXC2, PTPN11, and INTEGRIN α9/β1, contribute to the genetic-related subset of these fetal chylothorax cases. The speaker reported the first link between human fetuses having chylothorax with mutations in the INTEGRIN α9 (ITGA9) gene in 2008. The speaker’s group also recently reported a case of Noonan syndrome who responded very poorly to antenatal pleurodesis. In this lecture, the speaker will give an overview of fetal chylothorax including its pathogenesis and the rationale of the modalities available in fetal interventions that may be justified to improve the perinatal outcome. A series of publication in periodicals such as Fetal Diagn and Therapy, Ultrasound Obstet Gynaecol, Prenat Diagn, and Lymphology from the speaker’s group will be presented.
Mutations in the acetylcholine receptor pathway and fetal akinesia deformation sequence disorders (FADS)

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FADS is a frequent condition affecting about 1 in 3,000 pregnancies. Impaired fetal movement results in a spectrum of problems including growth retardation, fetal hydrops, pulmonary hypoplasia, and joint contractures.

Mutations in the acetylcholine receptor (AChR) pathway are one of several possible causes of FADS. Early diagnosis can be life-saving for some of the babies born with contractures and breathing problems. Depending on the type of mutation they could benefit from medication such as acetylcholine esterase inhibitors. Since early clinical diagnosis of a myasthenia-related condition is sometimes difficult in newborns, molecular genetic analysis provides an additional diagnostic tool.

FADS-relevant mutations have been found in a number of AChR components so far, including its several subunits (α1, β1, δ, γ, ε) as well as in receptor-related proteins such as rapsyn and DOK-7. A combination of clinical and molecular data helps to predict the clinical course and prognosis of the disease as well as to guide a targeted therapy.

The manifestation of FADS can be extremely variable even within the same family, ranging from early miscarriages, pre- or perinatal death to affected surviving sibs with contractures. Therefore, clinical and molecular data from prenatally deceased siblings may be crucial to elucidate severe phenotypes of AChR pathway mutations.

In summary, AChR pathway mutations contribute to a broad spectrum of intrauterine phenotypes and should be considered in patients with recurrent spontaneous abortions, fetal akinesia, hydrops, pterygia, or inborn contractures.
The placenta is believed to play an important role in the pathogenesis of preeclampsia (PE). The classic pathophysiological hypothesis in preeclampsia is that trophoblast invasion of spiral arteries is either very superficial or absent in preeclampsia, leading to reduced placental perfusion. This ischemic model cannot, however, be the single cause of preeclampsia since not all placentas from preeclamptic pregnancies show signs of ischemic lesions and epidemiologic studies have not shown any conclusive results regarding an absolute association between preeclampsia and poor fetal growth. More recent insights into the pathogenesis of preeclampsia supports a hypothesis of heterogeneous pathogenic pathways and the condition is more and more frequently regarded as a multifactorial syndrome.

To better understand the role of placenta pathology in preeclampsia we developed the concept of placenta functional morphology/pathology that today includes correlation between both umbilical and uterine Doppler findings and placenta morphology. In addition we have developed an ischaemic score (IS) for a more objective assessment of ischaemic lesions. IS was defined as the sum of all histological ischaemic lesions observed in the available parenchymal sections for each placenta. Ischaemic lesions were registered following the principle of 1 point for the presence of each lesion in each section. Several similar lesions observed in the same section still counted as 1 point. An abnormal IS was defined as \( \geq 1 \) (IS 0-1: mild; >1-3: moderate; 4+: severe changes). Cases with highest ischemic score (4 +) are delivered earlier in their pregnancy together with highest percentage of growth retarded infants. Notwithstanding, a significant number of PE placentas fail to show noteworthy ischaemic or other morphological changes that could explain the role of the placenta in the development of preeclampsia. It therefore seems, as if preeclampsia does not simply arise from a single pathophysiological mechanism, but from a variety of causes.
Lessons learnt from placental examinations in monochorionic twin pregnancies

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Monochorionic twin pregnancies have an increased risk of adverse outcome as compared to their dichorionic counterparts because of the almost ever-present vascular anastomoses that connect the two fetal circulations. These account for some unique complications, such as the twin transfusion syndrome, the twin anaemia polycythaemia syndrome and the twin reversed arterial perfusion sequence. Other complications are not unique to monochorionic gestations, but because of the shared circulation, they require a different management, such as intrauterine demise of one twin, discordant growth and discordant anomalies. Placental examination and injection studies contribute to a better understanding of these complications and help to improve their management.
Placental findings that may be predictors of neurocompromise

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Broadly categorized as early (<32 weeks gestational age) and later (>32 week gestational age) placentas, patterns have emerged with sound associations with neurocompromise in the individual, at least retrospectively. Data from early placentas is more convincing, with the inherent strong risk factor of prematurity and all the medical issues that arise with that alone. Early placentas with features of severe and prolonged ischemia (weighing <5\textsuperscript{th} percentila, infarcts, hypermaturity, decidual vasculopathy and atherosis) or severe, diffuse acute villous edema are well documented to be associated with clinically significant neurodisability in the infant. High fetal stage and grade findings of inflammatory disorders have also been seen to be associated with neurocompromise. Later placentas have less well substantiated findings usable to suggest risk for neurocompromise and include the same diagnoses as those in the early group with others most commonly associated with this age group including prolonged meconium exposure (meconium myonecrosis) and fetal thrombotic vasculopathy. All findings affect placental reserve, less reserve equates with lower tolerance to the intermittent anoxia with labor and also the ability to withstand what would be innocuous insults to a “normal” placenta. Studies showing the placental findings associated with neurocompromise have relied primarily on retrospective analyzes of placentas that have been brought to lawsuit. This being an obvious ascertainment bias that is difficult to control for, despite earnest measures. All findings are best reserved as “candidates” for prediction and caution should be used in reporting them to current cases.
Recent developments and issues in gestational trophoblastic disease

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Gestational trophoblastic neoplasia (GTN) encompasses several entities including complete (CHM) and partial (PHM) hydatidiform mole (HM), malignant choriocarcinoma (CC) and placental-site trophoblastic tumour (PSTT). HM are genetically abnormal, non-viable conceptions, which are associated with significantly increased risk for development of complications due to persistence of abnormal trophoblast (persistent GTN; pGTN), which occurs following 15% of CHM and 0.5% of PHM. Diagnostic histological features of HM are present in the first trimester but these features are now recognized to differ from those traditionally described in the later second trimester. The characteristic morphological findings of early HM include aspects of villous dysmorphism and abnormal villous trophoblast hyperplasia, with other specific features allowing reliable distinction between CHM and PHM. Rare familial biparental mole syndrome is now recognized associated with NALP gene mutations. The differential diagnosis of an apparently normal fetus with a mole can be complex, the main entities including twin pregnancy with mole and co-twin, mosaicism for mole and placental mesenchymal dysplasia.
How is placental morphology related to oxygen concentrations?

Berthold Huppertz

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Throughout the course of gestation the placenta is exposed to varying oxygen concentrations. During the first trimester the embryo lives in a low oxygen environment (below 20mm Hg) since maternal blood through the intervillous space of the placenta is not yet established. Only after 12 weeks maternal perfusion of the placenta starts increasing the oxygen concentration to about 50 to 60mmHg staying at about this level until delivery. Placentas from high altitude and placentas from animals under chronic hypoxia reveal that the placenta is able to adapt to changes in oxygen concentrations. The organ displays a higher degree of vascularization associated with branching angiogenesis. In the human placenta this results in an increased branching pattern of chorionic villi.

Severe cases of IUGR with absent or reversed end diastolic flow in the umbilical arteries (AEDF and REDF) lead to respective changes of placental morphology. The reduced flow towards the fetus results in a placental hyperoxia followed by a morphological adaptation of the placenta: decreased numbers of villous branches, reduced trophoblast surface and a wide intervillous space. This is extremely bad for the fetus, which suffers more and more from hypoxia due to the decreased surface area of the villi and thus the decrease in oxygen delivery to the fetus.

The morphological adaptation of the villous trees takes about one week. Thus a detailed analysis of the placental morphology after delivery may give an indication of the oxygen supply in the last period of gestation.
Promotion of banked donor milk in preterm infant feeding: is it a human rights issue?

Sertac Arslanoglu

Milan, Italy

Early in life, feeding preterm infants with breastmilk is the most effective dietary intervention for the prevention of infections and necrotizing enterocolitis with a potential of improved cognitive, cardiovascular and metabolic outcomes at long term (Arslanoglu and Moro 2009, Schanler 2007, Italian Guidelines for Human Milk Banking 2007). Hospitals and physicians are advised to recommend human milk for preterm and other high-risk infants either by direct breastfeeding and/or using the mother’s own expressed milk (AAP Section on Breastfeeding 2005). Banked donor milk is preferable to other supplements when the mother’s own milk does not meet the infant’s requirements (Academy of Breastfeeding 2007).

In countries where national policy focuses to improve infant health outcomes, banked human milk has been considered, since a long time, a reasonable and effective tool in the delivery of health care to infants and children. (Arnold 2006). But in some countries, skepticism about the nutritional and immunological quality of banked donor milk and concerns regarding infections transmission have limited its diffusion as a standard care.

The purpose of this paper is to present the proven clinical benefits, and the discovered facts about the nutritional and immunologic quality of banked donor milk. Clinically, the use of donor milk has been shown to prevent necrotizing enterocolitis (NEC) in the population of premature infants (Boyd 2007, Lucas 1990), to reduce healthcare costs,(Arnold 2002, Wight 2001), to decrease the long-term sequelae and costs from NEC, and give premature infants a better start in life.

In conclusion growing evidence has placed the human milk banking in a human rights framework. Banked donor milk should be a part of our health care in NICUs, and promoted.
Breastfeeding and later health

Mary Fewtrell

London, UK

The short-term benefits of breast milk, notably reduced risk of infection, are well recognised and are greater for infants born preterm than those born at term. Evidence also suggests that early nutrition via breast milk feeding may also have beneficial effects on long-term health and cognitive outcome. However, evaluating this is not straightforward. It is impractical and unethical to randomise healthy term infants to be breast or formula-fed and consequently the majority of data comes from observational studies which are subject to confounding. Nevertheless, there are two experimental studies in this field; one in preterm infants born in the 1980s in whom it was ethical and practical to randomly assign early diet; and the other a cluster randomized trial of a breast-feeding promotion intervention conducted with term mother-infant pairs. Both observational and experimental studies have strengths and weaknesses, and a combination of data from these approaches may provide the most accurate overall assessment of the long-term health effects of breastfeeding.

Two recent systematic reviews/meta-analyzes have considered evidence for the long-term health effects of breastfeeding. When considered together with data from the two experimental studies, evidence for a long-term beneficial effect of breast milk is currently most compelling for later cardiovascular risk factors, including blood pressure, blood lipids and obesity risk. Increasing evidence also supports the hypothesis that this effect may be mediated by the slower early growth pattern seen in those who receive breast-milk compared to infant formula. The effect of human milk on later cognitive outcome remains more controversial. Although several studies, including follow-up of the term experimental cohort, have reported a positive effect, other studies with adjustment for maternal IQ suggest that the effect is attenuated or abolished.

Further progress in this field would be aided by greater standardization between studies of factors such as subject selection, definition of breastfeeding, choice of outcome measures and, importantly, measurement of and adjustment for recognized confounders.
Feeding growth restricted preterm infants

Luca Maggio

Rome, Italy

Preterm infants usually receive similar postnatal nutritional intakes; however it is reasonable to consider whether specific supplies of macro and micronutrients would improve growth and main clinical outcomes in the intrauterine growth retarded (IUGR) newborns that already have suffered prenatal adaptations that might produce unique nutritional needs. In these infants, nutritional intakes lower than standard recommendations will continue to produce growth restricted infants with limited growth capacity, particularly of the brain and its many essential functions. On the other hand, IUGR could be associated with decreased pancreatic development, low insulin secretion, and decreased capacity for amino acid synthesis; it is possible, therefore, that nutritional intakes higher than standard recommendations could be less tolerated and might not sustain the same growth rate as in a normally growing fetus born preterm. Moreover, abnormalities of splanchnic blood flow could persist after birth giving physiological justification for a delayed and cautious introduction of enteral feeding. Such a policy exposes infants to the several risks of parenteral nutrition and to the negative effects of lack of enteral nutrients. The current literature is controversial and does not provide reliable guidelines; most studies have not distinguished between low birth weight, SGA and IUGR infants and further investigations should be performed before recommendations about parenteral and enteral nutrition for the particular subgroup of IUGR infants can be made.
Fortification of human milk in VLBW infants feeding

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Fortified human milk (FHM) fed infants continue to grow slower than preterm formula (PT) fed infants. Since slow growth is a marker of inadequate nutrition with the potential of neurocognitive impairment, further refinement of HM fortification models is warranted. Shortfalls with standard human milk fortification: The primary limiting nutritional factor, responsible for growth failure in preterm infants, is the suboptimal protein intake. Standard fortification does not solve the problem of protein undernutrition. So, novel fortification models should be devised in a way to deal with the problem of ongoing protein undernutrition. Individualized fortification approach has been shown to be effective in improving the protein intake and growth.

Novel approaches and proposed models for optimization of human milk fortification: individualized fortification.

Individualized fortification is now believed to be the best solution to the problem of the large variability of HM composition. Currently, there are two proposed methods for individualization: the first, targeted fortification, is depending on milk analyses; the second, adjustable fortification, is depending on the metabolic response of each infant.

Targeted fortification: The concept is to analyze human milk and to fortify it in a way that each infant receives the amount of nutrient that he needs. This method has been proposed by Polberger et al. and provided the preterm infants with improved protein intakes and growth. The milk is analyzed periodically and a target protein intake is chosen according to the predefined requirements of preterm infants. The amount of fortifier is added according to the protein content of HM to reach the targeted protein intake (3.5 g/kg/day in the study of Polberger).

Adjustable fortification: Protein intake is adjusted on the basis of the infant's metabolic response, evaluated through periodic determinations of blood urea nitrogen (BUN). This model is effective in providing the preterm infants with adequate protein intakes and appropriate growth approximating intrauterine intakes and growth. The adjustable fortification does not make any assumption regarding an infant's protein requirements, but it takes into consideration the metabolic response of the infant based on the actual protein status. Moreover, it does not need milk analyses and expensive equipment, and it is not labour intensive: in other words, it is extremely practical for routine use in the nurseries.

Conclusion: Fortification of HM, though is crucial, has become more complex than anticipated. Current standard fortification methods have yielded intakes resulting in slower growth compared to preterm formulas. Improvement of outcomes depends on models dealing with the large variability of HM composition and able to solve the problem of protein undernutrition. Individualized fortification has been proven to be effective to cope with this problem.

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Feeding the premature infant: Anything new to be added?

Manuel Sánchez Luna

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Feeding the premature infant is challenging due to its effect on growth and development and also on problems related to immaturity, as BPD and NEC. Excessive amounts of fluids during the first days of life has been proposed as a promoting factor of BPD, but controlled trials have a high variability of designs and do not demonstrated this relation. Early and aggressive feeding has been proposed to prevent metabolic shock and induce better growth but there are no data to support any effect decreasing BPD. Recent data support a beneficial effect of early-administration of intravenous lipids, and high doses of Vitamin A given intramuscularly during the first weeks of life has demonstrated a benefit decreasing BPD in newborns with a birth weight of less than 1,000 grams. Other nutrients have demonstrated no effect in preventing the development of BPD. So even a close relationship between nutrition and lung growth is proven, there are no well clinical trials in human designated to show how nutrition acts, being necessary more trials to better define how we can decrease chronic lung injuries in preterm newborns improving nutrition.

Breast feeding prevents infection from the GI tract and also reduce the risk in NEC development, but also prophylactic enteral probiotics has been proposed, by enhancing the immune responses of the host, to play a role in reducing NEC and associated morbidity. L reuteri improved gastrointestinal motility in preterm infants. B Lactis improved somatic growth in preterm infants treated with antibiotics. Recent studies demonstrate that the use of oral probiotics may improve gastrointestinal tolerance in infants weighing >1000g, but there is still not enough evidence about the possible benefits and potential adverse effects in the highest risk population to develop NEC, those with a birth weight below 1,000 grams.
Acceleration of maturity of immature gut prevention of necrotising enterocolitis

Nilgün Kültürsây

Necrotizing enterocolitis (NEC) is the most common severe gastrointestinal emergency in the NICUs. Prematurity is the most consistent factor and NEC risk is inversely related to birth weight and gestational age. Not only the complications of NEC but also withholding the feeds for long periods with the fear of NEC cause to postnatal malnutrition in preterm infants.

Immaturity of intestinal motility and digestion, circulatory regulation, barrier function and immune defense together with genetic predisposition, abnormal bacterial colonization and rapid advance of feeds lead to this devastating problem. Decreased motility causes to bacterial overgrowth and immature gut is also more permeable for bacteria. Immature intestinal innate immune system predisposes the preterm infant to intestinal injury. Immature immune response with increased inflammatory mediators such as PAF, TNF-α, interleukins and reduced anti-inflammatory capacity lead to the intestinal damage. This exaggerated proinflammatory response may be secondary to PRR signaling.

The balance between vasoconstriction and vasodilatation in the immature intestine is also problematic. Intestinal epithelial integrity may be regulated by prostaglandins, nitric oxide (NO), and epidermal growth factor (EGF). Preterms are commonly deficient in arginine which is an NO precursor. Recent studies indicate that infants with NEC have decreased endothelial nitric oxide (NO) synthase activity and decreased arteriolar NO production, which may predispose premature intestines to ischemic injury.

Abnormal bacterial colonization of gut due to increased use of antibiotics and frequent nosocomial infections in this vulnerable group of infants is also related to increased risk of NEC. Gut associated lymphoid tissue (GALT) is an important immune system in humans. Early colonization of neonatal gut with friendly bacteria and the signals from these commensal microbiota help to train these immune cells to discriminate the pathogens and harmless bacteria in the intestinal lumen, properly modulate adaptive immune response and also help to gain the ability of repairing the epithelium injured by inflammation and infection. These commensal bacteria have very important roles on nutrition, angiogenesis and intestinal immunity. However soon after birth the sterile gut of preterm infants mostly are colonised with nosocomial pathogens instead of bifidobacterial flora due to caesarean delivery, NICU pathogens, the problems of having human milk in the early days and the frequent antibiotic use.

Preventive strategies include human milk feeding, conservative feeding regimens and trophic feedings. Preterm mothers’ milk has less amounts of PAF probably due to increased PAF acetyl hydrolase and therefore preterm human milk may be superior to mature milk. Human milk has hormones, antiinflammatory cytokines such as IL-10, also growth factors and nucleotides that induce intestinal mucosal barrier development and maturation of intestinal functions.

Acceleration of maturation in the immature gut with the arginine, glutamine, IgA, EGF, IGF, erythropoietin and the use of probiotics, prebiotics seem also promising. Arginine, the sole NO precursor and glutamine an important specific fuel for enterocytes are found helpful for prevention of NEC, IGF-I protects intestinal mucosa from necrosis and apoptosis from intestinal H/R injury. rhEPO has been found to play a role in intestinal development, cell migration and intestinal restitution. rhEPO decreases intestinal lipid peroxidation and intestinal tissue damage after hypoxia and ischemia.

Dietary n-3 fatty acids alter PAF and LB4 production in the intestine and may have a protective effect against NEC. Probiotics such as S.boulardii, lactobacillus and bifidobacterium species have been found to decrease the NEC incidence and severity.

Probably a combined method of prevention may help to accelerate the gut maturation and protect the immature gut from NEC and its severe consequences.

Feeding the preterm infants will be much more optimal in the early days, weeks of life if this problem is solved.
Nutritional management of the premature infant

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Considerable progress has been made in recent years in the nutritional support of VLBW infants. Advances have been particularly dramatic in the area of parenteral nutrition, where the previously common delays in initiation have been eliminated and starting doses of amino acids have been increased to where they are mostly adequate. Advances in enteral nutrition have been more slow, largely because perceptions linking early feedings to the causation NEC have proven difficult to overcome. Overall, the necessity to provide adequate nutrition if neurocognitive development is to proceed unimpaired is now widely recognized. Nutrient intakes needed to achieve normal growth are summarized in the Table.

<table>
<thead>
<tr>
<th>Infant body weight (g)</th>
<th>500-700</th>
<th>700-900</th>
<th>900-1200</th>
<th>1200-1500</th>
<th>1500-1800</th>
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<tbody>
<tr>
<td>Weight gain of fetus (g/d)</td>
<td>13</td>
<td>16</td>
<td>20</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>(g/kg/d)</td>
<td>21</td>
<td>20</td>
<td>19</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Protein, required intake (g/kg/d)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral</td>
<td>3.5</td>
<td>3.5</td>
<td>3.5</td>
<td>3.4</td>
<td>3.2</td>
</tr>
<tr>
<td>Enteral</td>
<td>4.0</td>
<td>4.0</td>
<td>4.0</td>
<td>3.9</td>
<td>3.6</td>
</tr>
<tr>
<td>Energy required intake (kcal/kg/d)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral</td>
<td>89</td>
<td>92</td>
<td>101</td>
<td>108</td>
<td>109</td>
</tr>
<tr>
<td>Enteral</td>
<td>105</td>
<td>108</td>
<td>119</td>
<td>127</td>
<td>128</td>
</tr>
<tr>
<td>Protein/Energy (g/100 kcal)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral</td>
<td>3.9</td>
<td>3.8</td>
<td>3.5</td>
<td>3.1</td>
<td>2.9</td>
</tr>
<tr>
<td>Enteral</td>
<td>3.8</td>
<td>3.7</td>
<td>3.4</td>
<td>3.1</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Parenteral nutrition: Parenteral nutrition is indicated in the great majority of VLBW babies. It should start right at birth (within 2 h) and should continue until enteral feedings provide >90% of required intakes. The dose of amino acids should be no less than 3.0g/kg/d. Lipids should be started within 1-2 days of birth as a source of energy and of the essential long-chain PUFAs.

Enteral nutrition, early: The purpose of initial feedings (trophic feedings) is to prod the immature gut into maturity. Gastric residuals are important markers of gut function and are useful in monitoring gut maturation and guiding feeding advancements. Cessation of feedings should be imposed only if there are clear signs of NEC.

Enteral nutrition, late: Even with current routine nutrient fortification, protein requirements cannot be met because commercial fortifiers contain too little protein. It is therefore necessary to provide additional protein from a suitable source. Failure to do so leads to postnatal growth failure, which is associated with poor neurocognitive development. Formulas for premature infants lead to better growth than fortified mother's milk, but at the price of an increased risk of NEC.
Telemedicine in perinatal health care

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Telemedicine is the use of electronic information and communications technologies to provide and support health care delivery by connecting patients and health care providers who are separated by long distances. Recently, the term telehealth has risen as a favorable expansion upon the word telemedicine; telehealth includes non-clinical services such as medical education or research. Telehealth can prevent uncomfortable delays, high travel expenses and family separation by bringing specialized medical care directly to the people who need it. It is being practiced in rural areas, school districts, home-health settings, nursing homes, cruise ships, and on NASA space missions.

Telemedicine has many additional applications:
- Many hospitals offer public health awareness information through hospital-based medical web sites. And many health providers have partnered with cable television to offer extensive public service programming on health care issues.
- Hospitals and outreach clinics routinely use their in-house telecommunications networks to provide routine consultation services and continuing education training on new medical procedures for their staff, and to improve administrative processes. Emergency vehicles are often enhanced by onboard computer systems that use Geographic Information Services Technologies to direct ambulances to the patient by using satellite coordination, software programs, and wireless technologies. These state-of-the-art ambulances can instantly access patient information and allow emergency personnel to talk directly with physicians while the patient is en route to the hospital.

Telemedicine in Perinatal medicine:
- Perinatal care telemedicine can be used to monitor antenatal care, instruct regarding referrals, plan delivery care, help out in resuscitation of the newborn, essential newborn care and follow up of newborn health care, consultations and immunization.
- Regular health education to mothers, teleconferencing regarding consultation, continuing medical education, skill transfer, liaising regarding transfer of patients can all be performed by appropriate use of telemedicine.

Some of the issues to be considered:
1. Standards of practice in the use of telemedicine.
2. Licensed to practice across geographic areas
3. Privacy, confidentiality, and patient information security are critical issues.
4. Medical insurance and reimbursability.
Infant mortality in the era of globalisation: Where do we go from here?

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It is now clear to us that in the current era, efforts to decrease infant mortality will have to incorporate interventions that focus their effects on infants during the first month of life. We know that approximately 4 million infants are dying in the first 4 weeks of life worldwide and that 99% of these deaths occur in less developed countries. We are also aware that the bulk of research dollars set aside to improve survival in this age group is directed towards the 1% of infants in developed countries. Because globalization impacts all countries independent of their level of development, but not in an equitable manner, it is possible that less developed countries will be unable to meet the current challenges delineated in the millennium developmental goals due to a slowdown in their internal economies as a consequence of the current global financial crisis. The current events should lead the world health community to re-evaluate its current strategies and recommendations in order to introduce novel evidence-based approaches aimed at decreasing neonatal mortality within the context of the current global socioeconomic restrictions. Efforts to promote grass-roots movements and multidisciplinary health teams that address the problem of neonatal mortality in areas with endemic and epidemic rates may have the most profound short term effects if supported appropriately by local governments, high income countries, and the global industry. Promotion of local research capacity that is sustainable and addresses the primary healthcare needs of this vulnerable population has the greatest potential to impact in the long term infant mortality.
Impact of war and conflicts on perinatal health

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War, catastrophic events and disastrous circumstances can affect perinatal health. Our study reviewed most commonly encountered problem dealt during special events whether due to natural disasters like hurricanes, earthquakes, tsunamis, floods, tornadoes... or war and civil conflicts. Data and facts are retrieved from events worldwide and especially encountered in Lebanon. Psychiatric impact is important: mental diseases sexual abuses physical aggressions will be reviewed starting with a Lebanese study dealing with PTSD and drug abuse and dependency. About 10% of all children and adolescents meet full criteria for PTSD, MDD or SAD one year after war exposure and pre-war disorders, family violence factors and witnessing war events are powerful predictors of persistence of disorders. Sexual and child abuse as well as child labor has witnessed in increased frequency following war or catastrophic events. According to IOM 100 million children worldwide are submitted to sexual abuse and prostitution. 50% of children refugees in Africa estimated to 1.4 million were submitted to sexual abuse. It seems that real cause is more delocation, promiscuity and loss of family structures then directly war.

Pregnancy of the adolescents will also be reviewed and especially in areas of conflicts together with stress and complications of pregnancies. In countries like Egypt, 50% of women have been once aggressed and abused by their husband. 47% of women between 15 and 49 years are subject to domestic violence and 7% of them have been raped by their husband. In Lebanon, foreign worker suicides every week because of bad treatments by their employers, according to Human rights watch. According to Navy Pillay UN Coordinator for Human rights, violence against women is endemic in areas of conflicts and war. In Iraq for example due to war more than 80 widows of war have committed suicide attacks, convinced that this was the best solution for their problems. In Bosnia- Herzegovina in 1992, rape was a war strategy to destroy the bases of the society. In Kivu massive rapes started in the war in 1996, and according to WHO, 100,000 women were raped in 2004–2005, and in 2006, 28,000 of adolescent girls were raped and in June 2008 in North-Kivu 73 young girls are raped everyday with an average of 2200 cases in June 2008 according to an NGO International Rescue Committee. Moreover during war, new pathologies are encountered due to blind shelling, cluster-bomb, napalm and phosphorus, bombed cars and can lead to burns and trauma, permanent disabilities, and dislocation of families and NICU should learn to treat and be ready to receive this kind of patients. Lack of fuel and electricity, inadequate transport or bad storage of medications and vaccines can all lead to unfortunate events and inadequate management of pregnancies and deliveries. This situation may require new ways of management among them original calendar of vaccination. More than 250,000 child soldiers are a phenomenon that is still prevalent in more than 18 countries. Child soldiers are obliged to kill sometimes relatives are used as sexual object, and rehabilitation is very difficult. Principles of Paris were approved by 58 nations in 2007 and will help preventing this phenomenon. Child labor is also a goal.
Challenges of feeding low birth weight infants in resource restricted settings

Fred Were

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The nutritional needs of Low Birth Weight (LBW) Infants are now well established and known to be significantly higher than their term counterparts. It is also known that all newborns require to commence nutritive feeding within hours of birth. In bigger, more mature, infants this is usually possible through early breast or artificial feeding. Because LBW infants are often sick or deemed unstable at birth early enteral feeding is often thought to be unsafe. If early feeding is not instituted LBW infants will remain in a catabolic state leading to a daily loss of one gram (g) of protein/kilogram (kg) of their birth weight/day (d). In well resourced units such infants will be commenced on parenteral fluids providing all their macro and micronutrient requirements. This allows time for the infant to recover and be ready for milk feeding. Total intravenous feeding is an expensive and highly skill demanding intervention that remains un-available in poorer countries. The first challenge in nutrition for the LBW infant with restricted funding is therefore, “Safe enteral feeding during this early period of instability”. This stage may last up to 2 weeks. Innovative strategies are required here. This paper will cover some evidence based strategies for safe early enteral feeding of LBW infants.

Low birth weight infants fed enterally require an intake of 3.6-4g/kg/d and 120kcal/kg/d of protein and energy respectively to facilitate normal growth and account for gut losses. It is therefore essential that the milk given fulfils these requirements within tolerable volumes. Breast milk (especially after the 2nd week of lactation) and standard formula have about 1g/100ml of 67 kcal/100ml of protein and energy respectively making it virtually impossible to provide the required nutrients within safe volumes of these preparations. Breast milk fortification (BMF) and preterm formula milk (PTF) can circumvent this but they too are costly.

This brings in the second challenge for underfunded feeding programs for the LBW infant; How to improve the nutritional value of milk for LBW infants affordably. The first strategy is the maximal utilization of the mothers’ natural premature breast milk (PBM) during the first two weeks of lactation. The median protein and energy content of PBM is 2g/100mls and 70kcal/100mls respectively making it capable of safely providing adequate nutrients whilst it is available. Unfortunately most mothers’ milk assumes the mature variety by or soon after 2 weeks of lactation when most small infants still need it. Storage of surplus PBM for later use offers some promise if such facilities are available. The final challenge that this paper/presentation addresses is “how to rationalize the use of BMF and PTF” within the restricted cost constraints. The options include deliberate BMF or use of PTF for those at highest risk of or already experiencing growth failure. Another option involves mixing of mother’s and PTF to achieve a middle ground between ideal and available.

Though the challenges of adequate nutrition in LBW infants when funding is restricted are enormous simple manipulations of available technology should be able to narrow the gap.
The role of surfactant as an etiological factor of RDS is well known. Besides the surface activity, several components of the surfactant are involved in the innate immunity. The fact that surfactant is secreted into the amniotic fluid makes it as an interesting candidate that influences the premature birth, particularly in pregnancies complicated by chorioamnionitis. Surfactant associated collectins, surfactant protein A (SP-A) and SP-D are well known proteins that bind several microbes, influence phagocytosis by alveolar macrophages, and have pro- and anti-inflammatory roles. We have studied the roles of lung collectins using two approaches: 1. transgenic mice expressing either SP-A or SP-B are studied in the setting of LPS-induced preterm birth; 2. the association of SP-A and SP-D polymorphism with the susceptibility to preterm birth is studied. Preliminary results are presented. In addition new results on the role of SP-C in preterm birth are shown. According to preliminary evidence certain SP-C gene (SFTPC) polymorphisms associate with lung diseases and very preterm birth (Lahti et al. Eur J Hum Gen 2004;12:312-20).

Aims: We investigated the association of SFTPC single nucleotide polymorphism (SNP) rs4715 with factors affecting spontaneous preterm birth and characterized the SP-C expression in human and mouse gestational tissues.

Methods: SFTPC SNP rs4715 polymorphism was genotyped in a homogeneous Northern European population of mothers and infants in spontaneous preterm birth and term controls. The expression and protein of SP-C in gestational tissues was analyzed.

Results: SFTPC SNP rs4715 did not associate with spontaneous preterm birth. However, fetuses with short interval (< 72 hours) between preterm premature rupture of fetal membranes (PPROM) and preterm birth had significant overrepresentation of the minor allele A, whereas in fetuses with prolonged PPROM (≥ 72 hours) the frequency was decreased (P<0.0001). Maternal SFTPC did not associate with the duration of PPROM.

SP-C mRNA and proprotein were detected in fetal membranes, placenta, and pregnant uterus.

Conclusion: SFTPC SNP rs4715 associates with the duration of PPROM and SP-C is expressed in gestational tissues. We propose that fetal SFTPC either moderates the inflammatory activation or serves as an antimicrobial peptide protecting the extraembryonic compartment.
Surfactant therapy for respiratory distress syndrome

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Respiratory distress syndrome (RDS) is a significant cause of morbidity and mortality in preterm infants. Surfactant therapy has made a significant impact on the survival without increasing the cost per survivor. Animal derived surfactants (ADS) as well as synthetic surfactants without proteins have been extensively evaluated in preterm infants. ADS are more effective and decrease mortality when compared to synthetic surfactants. Three ADS commonly available globally include Survanta (beractant), Infasurf (calfactant), and Curosurf (poractant alfa). They differ in their composition, amount of phospholipids and plasmalogens, onset and duration of action, dosing volume, viscosity, need for additional doses, clinical outcomes, and cost effectiveness. Prospective as well as retrospective studies comparing beractant and calfactant have shown no significant differences in clinical or economic outcomes. However, comparison of beractant with poractant alfa in randomized trials have shown significantly faster weaning of oxygen, fewer additional doses, decreased mortality and cost benefits in favor of poractant alfa. Differences in mortality reported from 10 studies have shown that poractant alfa is the only animal derived surfactant with a significant reduction in mortality when compared with beractant or calfactant. A retrospective study involving more than 24,000 preterm infants has shown a significant reduction in mortality, length of stay, and total hospital costs with poractant alfa when compared to beractant or calfactant. These differences in outcomes may be related to the fact that poractant alfa contains greater amounts of phospholipids distributed in a smaller volume as well as a greater amount of antioxidant phospholipids, namely plasmalogens.
Pulmonary function in newborns with meconium aspiration syndrome

Marta Szymankiewicz

Poznań, Poland

Meconium aspiration syndrome (MAS) is one of the most frequent causes of respiratory insufficiency and morbidity among term newborns. Reduction of the incidence and severity of MAS became a new target for obstetricians and neonatologists. Pathologic examinations of lungs from newborns who died of MAS a deficiency of surfactant was found as a result of secondary damage of pneumocytes type II function and the inhibition of biophysical properties of surfactant. Inflammation and surfactant inactivation may finally result in adult respiratory distress syndrome as well as predisposition toward persistent pulmonary hypertension of the newborn, a complication that may require ECMO. Thus it has been proposed that surfactant replacement in MAS may reverse respiratory insufficiency. Previous studies showed that conventional surfactant administration reduces the severity of MAS and, thus, decreases the number of infants with progressive persistent pulmonary hypertension of the newborn requiring support with ECMO. Also, other studies support the thesis that diluted surfactant lung lavage is a safe and potentially effective therapy in the treatment of infants with MAS.

Pulmonary function in MAS and changes in pulmonary mechanics during treatment were not clearly described, and no objective values of pulmonary functions were used to assess the respiratory status. A lack of confirmed improvement of lung volumes may extend the duration of ventilation, prolonged exposure to high FiO2, and high inspiratory pressure resulting in an increase of occurrence of pneumothorax, intraventricular haemorrhage, and related complications. Surfactant lung lavage together with surfactant administration improved the elastic properties of the lungs, what is reflected by an increase of compliance (C), and decrease of airway resistance, mean airways pressure, ventilatory settings and oxygenation index. Surfactant lung lavage followed by administration of surfactant probably stopping migration of meconium and did not allowed to spread an obstructive changes in small bronchiolis and alveolar ducts.
Conservative methods in PPH: Uterine blood supply and hemostatic procedures

Jose M. Palacios Jaraquemada

Buenos Aires, Argentina

The use of hemostatic procedures promotes uterine conservation in the presence of different types of obstetric hemorrhage. However, its correct application depends mainly on prior knowledge of uterine irrigation and of its topographic distribution. There are two clearly defined vascular regions in the uterus: one which comprises the uterine body, named S1, and another which includes the lower segment, uterine cervix and upper portion of the vagina, S2. Vascular distribution delimits both anatomical areas. S1 is irrigated by the uterine arteries as well as by collateral branches of the ovarian and superior vesical arteries. On the other hand, S2 is irrigated by pelvisubperitoneal collateral branches of the internal pudendal artery and, to a lesser extent, by accessory vessels of the internal iliac, uterine and lower vesical arteries. Topographic knowledge of the bleeding is deemed essential when selecting a procedure. Even though most hemostatic techniques have been designed for the hemostatic control of S1, a number of them can be applied to S2 with certain limitations. The main technical restriction in S2 is the inadequate exposure of the pelvisubperitoneal space, a fact that limits its safe and efficient application. As it occurs with other uterine hemostatic methods, the appearance of coagulopathy or of uncontrolled shock reduces its efficacy significantly. In these cases, the use of simple, universal and efficient methods has made it possible to have enough time to revert the hemostatic and hemodynamic imbalances almost without bleeding.
Substance abuse among pregnant women is an area of special concern. Questions of paramount interest are the effects of drug use/misuse on the fetus, newborn and young child. To provide answers to these questions, investigations have examined teratologic effects, obstetrical complications, prenatal and postnatal delays in growth and development, and impairments in neurobehavioral functions. This presentation will provide an overview of existing research on the effects of illicit prenatal drug exposure on the growth and development of the newborn and young child. Perinatal outcomes, i.e. birth weight, head circumference, prematurity, and neurobehavioral characteristics associated with prenatal opioid exposure, including heroin, methadone, and buprenorphine; prenatal cocaine exposure; and prenatal methamphetamine exposure will be discussed. Neonatal abstinence related to opioid exposure will also be discussed. Studies that have examined the cognitive and developmental outcome of opioid exposed and cocaine exposed children through the first 5 years of life will be reviewed. The role of illicit drug exposure as a marker of environmental risk and the importance of utilizing an interactive environment of care model in delineating factors that may either exacerbate or attenuate risk will be discussed.
I illicit drug abuse places pregnant women at increased risk for medical and obstetrical complications. As a result, medical problems are seen in their neonates such as premature birth and intrauterine growth restriction and potentially sequelae such as developmental delays. In utero opioid exposure may be associated with abstinence in 60-90% of the newborns. Up to 70% of the women experience some symptoms of depression necessitating pharmacologic treatment with tricyclic antidepressants or the selective serotonin reuptake inhibitors, both of which significantly increase the risk of neonatal respiratory distress, hypoglycemia, neonatal convulsions and the occurrence of neonatal abstinence. Neonatal abstinence is described as a generalized disorder characterized by CNS hyperirritability, gastrointestinal dysfunction, respiratory distress, and autonomic dysfunction manifesting as vague symptoms such as yawning, hiccups, sneezing, mottled skin color, and fever. The onset of withdrawal symptoms varies from minutes or hours after birth to 2 weeks of age, but the majority of symptoms appear within 72 hours. Acute symptoms may persist for several weeks, whereas subacute symptoms (e.g., irritability, sleep problems, hyperactivity, feeding problems, and hypertonia) may persist for 4 to 6 months. About 50% to 60% of exposed infants demonstrate symptoms significant enough to require medication. To determine whether an infant will need pharmacologic treatment for withdrawal, appropriate assessment of symptoms is essential utilizing a scoring tool to monitor the onset, progression, and resolution of symptoms and to assess the infant’s response to pharmacotherapy. Recommended pharmacotherapy for neonatal abstinence includes a 25-fold dilution of tincture of opium or an oral morphine solution. The implications of maternal drug addiction on the newborn are preventable if women do not use dependence-producing drugs, licit or illicit, during pregnancy. Through intense educational efforts and appropriate treatment for addicted pregnant women, the desirability and availability of drugs may be thwarted. Unfortunately, the psychosocial and socioeconomic milieu of modern society continues to propagate dysfunctional families, victimization of women, and an intergenerational cycle of drug abuse.
Efforts in normalizing the lives of addicted pregnant women and their children

May Olofsson

Copenhagen, Denmark

Children born of substance using mothers are high-risk children. They are from the very beginning of fetal life exposed to a multitude of detrimental factors of both a biological and a psychosocial nature with severe consequences for their development. They are at risk of congenital malformations, low birth weight, premature born, intrauterine asphyxia and other severe complications during pregnancy and delivery. In the neonatal period they are at risk of neonatal withdrawal symptoms, infectious diseases and other neonatal morbidity and mortality. Many of these infants are furthermore growing up under chaotic and instable environments where they are suffering from neglect and abuse. All the above mentioned problems can be prevented by early and multidisciplinary intervention during pregnancy, delivery and the first years of life. Family Center in the University Hospitals of Copenhagen is a comprehensive prenatal and postnatal program for pregnant substance using women and their children up to the age of 6 years. The program has multidisciplinary staff of doctors, midwives, psychologists and social workers and offer comprehensive care for the pregnant woman, her partner and the newborn infant and follow up the children and the families to school age. From the early pregnancy Family Center collaborates very closely with the Social Services, General Practitioners and others in the Primary Health Care System. Family Center has dramatically reduced health problems, developmental disturbances, neglect and abuse in children born of substance using mothers in Copenhagen during the last ten years. The Danish Government has in 2008 decided to provide similar programs all over the country during the following four years. Methods Results and experience from Family Center in Copenhagen will be presented.
The implications of maternal drug addiction on the newborn

Loretta Finnegan

USA

Illicit drug abuse places pregnant women at increased risk for medical and obstetrical complications. As a result, medical problems are seen in their neonates such as premature birth and intrauterine growth restriction and potentially sequelae such as developmental delays. In utero opioid exposure may be associated with abstinence in 60-90% of the newborns. Up to 70% of the women experience symptoms of depression necessitating pharmacologic treatment with tricyclic antidepressants or the selective serotonin reuptake inhibitors, both of which significantly increase the risk of neonatal respiratory distress, hypoglycemia, neonatal convulsions and the occurrence of neonatal abstinence. Neonatal abstinence is described as a generalized disorder characterized by CNS hyperirritability, gastrointestinal dysfunction, respiratory distress, and autonomic dysfunction manifesting as vague symptoms such as yawning, hiccups, sneezing, mottled skin color, and fever. The onset of withdrawal symptoms varies from minutes or hours after birth to 2 weeks of age, but the majority of symptoms appear within 72 hours. Acute symptoms may persist for several weeks, whereas subacute symptoms (e.g., irritability, sleep problems, hyperactivity, feeding problems, and hypertonia) may persist for 4 to 6 months. About 50% to 60% of exposed infants demonstrate symptoms significant enough to require medication. To determine whether an infant will need pharmacologic treatment for withdrawal, appropriate assessment of symptoms is essential utilizing a scoring tool to monitor the onset, progression, and resolution of symptoms and to assess the infant’s response to pharmacotherapy. Recommended pharmacotherapy for neonatal abstinence includes a 25-fold dilution of tincture of opium or an oral morphine solution. The implications of maternal drug addiction on the newborn are preventable if women do not use dependence-producing drugs, licit or illicit, during pregnancy. Through intense educational efforts and appropriate treatment for addicted pregnant women, the desirability and availability of drugs may be thwarted. Unfortunately, the psychosocial and socioeconomic milieu of modern society continues to propagate dysfunctional families, victimization of women, and an intergenerational cycle of drug abuse.
Studies on the performance and the uptake of prenatal screening in Europe

Rosalinde Snijders

Groningen, Netherlands

Over the past 25 years different policies have been adopted in screening for fetal abnormalities. In some countries all pregnant women are offered prenatal ultrasound and/or biochemical testing whilst in other countries testing is only available to a high risk group. The main points of focus in the different screening programs have been neural tube defects and chromosome abnormalities. In this presentation national screening policies, uptake and performance will be summarized. Special attention will be paid to laws governing termination of pregnancy and the potential impact of the screening programs on perinatal death statistics.
Perinatal network for young researchers in the Netherlands including national and international studies and its impact on common guidelines, team work and malpractice

Hans Duvekot

Rotterdamm, Netherlands

One of the major fields of investigation within the Cochrane Collaboration is obstetrics and perinatology. Randomized controlled trials (RCTs) are momentarily the preferred methods to dissolve the efficacy and preference of different treatment options. In recent years already many national and international RCTs were performed. Dutch hospitals participated individually in most of these international trials, but nation-wide coordination was absent. Since the Dutch organization of the obstetrical care differs distinctly from that in the surrounding countries the Results of most of these international RCTs are often not directly implementable in the Netherlands. The need for a Dutch collaboration to perform large RCTs was strongly felt. The Netherlands is a densely populated country, has almost 17 million inhabitants and 200,000 deliveries each year. Dispersed over the country ten perinatal centers coordinate high care obstetrics in their region. The travel distances in the Netherlands are short and the perinatal centers are in close contact with each other. A number of these perinatal centers founded a research consortium in 2003. Funding of the first six RCTs was obtained from the Netherlands Organization for Health Research and Development. The Dutch consortium for studies in women's health and reproductivity has expanded since then. Many RCTs in the fields of obstetrics, fertility, neonatology, uroGynecology, gynecology and even gynecological oncology are performed. So far, eight obstetrical studies have been completed and Results were published in well established (obstetrical) journals. Twenty-one studies are still ongoing. The studies are coordinated by gynecologists in the perinatal centers. More than 50 other hospitals in the whole country participate in one or more of the RCTs. Participation of so many hospitals also promotes the implementation of the Results of the several trials. In future, we hope that this may lead to more safety and better care for our obstetrical patients.
Prevention of preterm birth – international cooperation of young researchers via FMF conducted multicenter-studies combining developing and developed countries

Ilka Fuchs

Berlin, Germany

The prevalence of preterm birth has not markedly changed over the last fifty years. Not a single country irrespective of the standard of its medical system or the effort and money willing to spend succeeded to significantly diminish the rate of preterm birth. It remains evident in both developed and developing countries.

There are two groups of patients at risk. Patients with singleton pregnancies presenting with a short cervix and patients with multiple pregnancies, in whom this condition itself is the major risk factor. In both groups several interventions have been investigated. While in singleton pregnancies some treatments seem effective such as the use of progesterone in those with a very short cervix, in patients with twin pregnancies no treatment has clearly been beneficial.

A promising approach to reduce preterm birth seems the use of a cerclage pessary. It is a non-invasive simple technique without major side effects. This medical device is all but new. It has been used for more than forty years in countries such as Germany. In others, however, the device is completely unknown. Astonishingly, no big high-quality studies have so far been conducted to prove or disprove its efficacy.

The Fetal Medicine Foundation London has been a leading example of the feasibility to build up international networks to perform studies powerful enough to give reliable answers and the importance to thereafter implement the new techniques together with a standard of quality throughout the world.

Regarding the use of pessaries for the prevention of preterm birth several studies are now under way including a multicentre trial conducted by the FMF London.

It will hopefully be another example, that the spirit of international cooperation is the best approach to forge important problems no one is likely to solve alone.
Fetal medicine can now be regarded as an accepted and important subspecialty in obstetrics. A large and still growing number of fetal structural, functional, genetic and acquired fetal abnormalities can now be diagnosed accurately. With advances in genetic testing, many more diseases are expected to be detectable before birth.

Most often however, each of these diseases itself is relatively rare. For studies on pathophysiology, only a few cases can be sufficient. For studies on accuracy of diagnostic tests, and even more for studies on therapeutic interventions, single centers most often see too few patients to obtain adequate sample sizes.

International multicentre studies running for long periods of time are likely the only option to complete adequately powered trials. This requires commitment from colleagues who may only deal with a handful of eligible pregnancies annually, and for whom this particular disease is not a main research subject. These and other large multicentre trials on the management of rare fetal disorders may benefit from international organizations such as the International Fetal Medicine and Surgery Society (IFMSS), North American Fetal Therapy Network (NAFTNET) and the Eurofetus initiative. Such networks may arrange or support web-based data-sharing facilities and funding to be used jointly by researchers studying rare diseases, helping each other to complete large scale projects.

In this presentation, the author will share his experience with successful and less successful international multicentre trials, and interactively discuss tips, tricks & pitfalls for those planning to organise such trials.
Labor monitoring without vaginal examination: New doors to open with non invasive tools

Jacky Nizard

Poissy, France

Non invasive tools, mainly based on ultrasound technology, are currently being developed to monitor fetal head progression during labor. The difficulty is to position fetal head in relation to the maternal pelvic bone. Two technologies are under evaluation. One technological option is to use a position-tracking system to determine fetal head position and maternal pelvis in space and subsequently combine both head and pelvis in a 3D model. The other option is to use only ultrasound images, with fetal and maternal landmarks. Both options assume maternal pelvis to be constant in shape and size.

The first system, using the position-tracking system, has been evaluated in multicentric studies and yields coherent data as much as fetal head position and station are concerned. It can use several methods of measurement of both position and station depending on labor progress and available ultrasound landmarks.

The second system, based on ultrasound only, has been independently evaluated by different teams. Data provided by these teams are close, but not sufficiently to consider homogeneous. What is most interesting is how information is used. In the first case, the system uses “clinical language”, i.e. the fetal head is +1 in OA for example. In the second case, the system gives new information, i.e. the progression angle is 125° thus the probability of vaginal birth is xx%.

Future is incredibly exciting and new systems might arise. We will probably see systems share their technology. But let’s not forget that once accuracy and reliability are achieved, we need to demonstrate usefulness. This will take time and large studies.
Strategies to reduce maternal mortality in developing countries – Steps and strategies making motherhood safer

H. Kaulhausen (1), H. Halle und Lisa M. Masterson (2)

(1) Remscheid, Germany; (2) Los Angeles, USA

Constructive and continuous policy on sexual and reproductive health:
Provision of condoms and modern contraceptives on the district levels (local health stations and centers).
Delegation of medical responsibilities to experienced midwives, traditional birth attendants and other paramedical personal (under supervision of Ministries of Health and/or WHO).
Prophylaxis of malaria as an important cause of intrauterine growth retardation.
Avoidance of unsafe and illegal abortions and of unwanted pregnancies.
Elimination of female genital mutilation (FGM).
Early operative therapy of vesicovaginal and/or rectovaginal fistula in specialized centers.

Concentration of high-risk pregnancy surveillance and obstetric care in secondary or tertiary referral hospitals.
Organization of transportation from district health stations to these facilities without unnecessary delay.

Education and training
Continuous training of health care workers in all levels (community, district and referral level), including participation of local people.
Postgraduate education of physicians in OB/GYN.
Consequently: early diagnosis of obstetrical risk factors and complications before, during and after birth.

Mobilizing financial resources providing more money for maternal health programs in developing countries, e.g.
WHO
World Bank
Foundation, e.g. Bill and Melinda Gates Foundation
Google.org, and other donors
Additional consequence: avoidance of “brain drain” (physicians, nurses, midwives and other medically skilled workers) from poor to rich countries.
Coordination and non-competitive development aid and technical assistance by NGO’s, by the international aid community and by the WHO.

Other factors leading to substandard care and delays
Inappropriate management by medical staff members: poor training, lack of treatment standards and guidelines, lack of medication and/or technical equipment like ultrasound.
Lack of prenatal and postpartum wards and of maternity waiting homes near the referral hospital.
Lack of registration and confidential enquiry of maternal and intrauterine fetal deaths.
Reduction of maternal mortality in a developing country

Corazon Yabes Almirante

Quezon City, Philippines

The Maternal Mortality Ratio in the Philippines was 172/100,000 live-births, in 1998 down from 203/100,000 in 1993, a reduction of 18%. Reduction by 50% was targeted in 1999 (86/100,000) in 5 years through the Women’s Health and SafeMotherhood Project (WHSMP), a project of the Department of Health and local government. 234 rural health units, barangay health stations, provincial and district hospitals, 92 obstetric 1st level hospital, 15 maternity waiting homes and 10 lying-in clinics were set. Obstetrical kits, micronutrients were given. Equipments, Instruments, Ultrasound Machines were distributed to selected provincial hospitals. Training of health-workers at the first level referral hospital on gender sensitive healthcare and emergency obstetric care was done.

In 1999, SafeMotherhood Taskforce was to identify the regions with the highest maternal deaths; lowest: contraceptive use, Iron and Iodine intake, age of first marriage, utilization of health facility, prenatal care, highest number of unskilled attendant at childbirth, strong religious beliefs and church influence in decision making. The First SafeMotherhood Congress held August 11 – 13, 1999 antedated the WHO summit in 2000 for the Millennium Development Goals. Davao Declaration: maternal death is not a medical problem but also a social concern; social, economic health and medical intervention must be jointly implemented; women empowerment is a basic strategy. 2006, MMR was 162.

International Agencies say that the Philippines have the slimmest chance to meet 55/100,000 MMR but hope is there. 1. changed strategy of the referral network (2006 –2012); 2. facility based childbirth by skilled professionals (economic crisis have stemmed the tide of health-workers exodus). 3. Social Workers, local government and NGO are partnering to bring women to health care facility. 4. Small private health care facilities specializing in family planning and childbirth services are now in place.
Can we predict or prevent preterm birth?

Roberto Romero

Detroit, USA

Preterm birth is the most important challenge to modern obstetrics and the leading cause of perinatal morbidity and mortality worldwide. The improved prognosis of preterm neonates is largely due to neonatal interventions. Antenatal steroids have been effective in reducing neonatal morbidity. Major advances in obstetrics are required to prevent spontaneous preterm labor and other disorders responsible for preterm birth. This presentation will argue that the current concepts that underpin the prediction and prevention of preterm birth need to be recast. Preterm birth is heterogeneous, resulting from spontaneous preterm labor (with intact or ruptured membranes), and indicated birth (preeclampsia and fetal growth restriction). Yet, each of these conditions represent syndromes with 1) different etiologies; 2) long preclinical phases; 3) phenotype definitions which are the cause of the disease; and 4) the result of gene environment interactions. We propose that the strategy for risk assessment and prevention of preterm birth needs to be based on the identification of the specific mechanisms of disease responsible for these syndromes. High-dimensional biology and systems biology offer new ways to define the mechanisms of disease and the taxonomy of obstetrical disorders responsible for preterm birth. The contributions of genomics, proteomics, metabolomics and systems biology to the understanding of preterm birth will be described.
Efficient measures to prevent premature birth at high risk

Erich Saling

Berlin, Germany

Introduction: Prematures born ≤32gw are at particular risk. Although many causes of premature birth are known, ascending genital infection is the most important avoidable one. The „protective lactobacillus system“ and the vaginal pH play a crucial role in the prevention. BV and/or ascending genital infection start often with a disturbance of this vaginal milieu. Our policy is not only to detect and treat vaginal infections, but already to detect and treat disturbances. Vaginal pH-measurement gives a first insight into this protective bio-system. When the pH is increased, further diagnostic measures – and if necessary therapy – have to follow. In order to detect these disturbances much earlier, we recommend that pregnant women themselves measure their pH regularly from the very start of pregnancy.

Results: In our study the rate of infants <1,500g was 1.3%. – in the previous pregnancy 7.8%. Results from Thuringia (Hoyme et cow): The rate of infants <32gw was 1.58% in the first half of the year 2000, and 0.99% in the second half, when the measure was employed. Both our study and Hoyme’s had some methodological shortcomings; the current study of German health insurance companies is more sophisticated as they used “propensity score matching”. The data are currently being evaluated. First provisional Results are encouraging.

Conclusion: We think that these studies are important first indicators that pH-measurement by the women themselves improves the perinatal outcome. Further research is necessary.

More information: www.saling-institute.org
Use and abuse of caesarean section – a transatlantic evaluation

Stephan Schmidt

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While the medical technique of caesarean section (CS) without doubt has saved numerous life’s in events such as obstructive labor or fetal distress its abuse for non medical reasons is widely discussed and criticized in developed countries. In the developing countries the lack of facilities as well as trained personal not available in case of obstetrical emergency imposes a heath care problem. Statistics: The transatlantic evaluation of perinatal statistics indicate a high variability of the percentage of birth by CS. The highest number of CS is performed in Central and South America (>30% of all birth) while the lowest figures are registered in surveys of the Atlantic coast of Africa (<5%). A transatlantic evaluation of the northern globe indicate progressive rising CS rates both in Europe and the US. In the United states a rapid increase of CS rates was reported in the 70s and 80s. Due to the set “goal 2000” a decline was thereafter obvious. Further on though the highest rates where reported (>30%) after the year 2005. In Europe the average CS rate is 19% with the highest rate in Italy (36%) and Portugal (>30%) and low in the Netherlands (<15%). Another area of large variation is the Caribbean were very low rates are reported from Haiti (<2%) and high rates Dominican Republic (>30%). Cesarean Section rates and heath indicators: WHO has stated that there is no justification for CA rates higher than 15%. This assumption was supported by a number of scientific epidemiologic surveys showing no further reduction of maternal mortality when CS was found to be >15%. The Cochrane Review on caesarean section for non-medical reasons at term identified no studies that met the inclusion criteria to prove scientifically the benefit of a wider use of CS. Some authors though had argued that CS would improve the later quality of live by preserving the pelvic floor during child birth.

Medical problems after Cesarean Section: A problem of placentation during further pregnancies (placenta parevia and percreta) as well as maladaptation of the child through wet lung disease and even the fact of potential laceration of the child during child birth by CS have been addressed. Litigation as an influence on CS rates: Litigation is a rising career problem both in the USA as well as in Europe. The load of rising numbers of cases at court and the rising compensations are reality in the UK and Germany while in other countries like the Netherlands, Switzerland and Scandinavia litigation is still infrequent. Figures of CS vary widely in Europe in a pattern that fits with these attitudes. While Scandinavia, and the Netherlands have low figures Germany and the UK show rising CS rates. Social Status: The low incident of CS is correlated to the social status. The odds of having an elective caesarean are lowest for woman living in the most deprived areas.

Cesarean Section for non medical reasons

CS on demand for woman has the potential value of the control of the process. This seems beneficial in the view of certain social groups. In the UK maternal request is the first most common reason for performing CS. The rate in central and south America is the highest with readings of double figures in some countries (70%).

Conclusion: The transatlantic evaluation of the use and abuse of CS show rising average values on both sides of the Atlantic ocean. Initiatives by governments to counteract this phenomenon up to now seem to have only limited potential. Medical cultures differ tremendously between European countries and obviously influence the rates of CS in otherwise comparable environments. Demographic changes such as maternal age as well a social circumstances have an independent influence on the likelihood of operative delivery.

CS rates at the Atlantic coast of Africa with very low figures demonstrate the danger of the lack of availability of the operative procedure in the most deprived transatlantic areas.
The evidence-based caesarean section – 20 years of experience with the Misgav Ladach method

Michael Stark

The New European Surgical Academy, NESA, Berlin, Germany

Surgical procedures should be standardized according to evidence-based facts concerning safety and outcome.

Such studies were done at the Misgav Ladach hospital in Jerusalem concerning caesarean section.

It was shown that the right-handed surgeon should stand on the right side of the parturient, this makes the delivery of the newborn's head easier, and the needle points away from the bladder while the uterus is being sutured.

The modified Joel-Cohen method was found to result in a shorter incision to delivery time, lower rate of febrile morbidity compared to the Pfannenstiel incision.

Opening the peritoneum by bi-digital stretching rather than with sharp instruments proved to be safe, and exteriorization of the uterus makes stitching easier and prevents unnecessary bleeding. Suturing the uterus with one layer rather than two results in stronger scars.

Closing the peritoneum prevents adhesions, and results in reduced need for painkillers.

The fascia is sutured continuously, first knot under the fascia to prevent irritation in the sub-cutis, and from the right to the left, which proved to be ergonomically correct.

For this method only 10 instruments and three sutures are needed.

Since the introduction of this method 20 years ago, over 40 peer-reviewed publications from different countries have evaluated this method. All showed various advantages of this method: shorter operation time, shorter hospitalization, quicker mobilization, less need for painkillers, less blood loss, lower rate of febrile morbidity and lower costs. These studies will be presented.

We recommend the Misgav Ladach Caesarean section as a universal routine method.
Reverse breech extraction in cases of impacted fetal head during second stage caesarean section

Dalia Schwake

The Holy Family Hospital, Nazareth, Israel

Introduction: Second stage Cesarean Section (CS) is associated with a higher risk of maternal morbidity especially in cases with fetal head impaction. The standard recommended procedure in these cases is to gently disengage the fetal head from the pelvis employing in some women a vaginal pressure to push up the impacted fetal head.

Objective: To explore whether a reverse breech extraction maneuver at second stage CS is feasible and to examine fetal and maternal morbidities employing this maneuver.

Setting: A community hospital.

Design: A prospective cohort study during a period of 3 years.

Patients: Women with urgent CS performed at second stage with full dilatation and fetal head impaction were recruited to this study.

Outcome measures: Estimation of blood loss, blood transfusion, drop of hemoglobin, need for J or inverted T shape incision, inadvertent extension of incision as well as postpartum hemorrhage, fever, scar infection and urinary tract infection. In addition, Apgar score at 1’/ 5’, umbilical cord PH, fetal trauma and admission to neonatal ICU.

Results: The total number of deliveries during the period of the study was 5,710. Of which 1,206 (21%) were performed by CS including 815 (14%) by emergency CS. Twenty five cases were performed at full cervical dilatation with an impacted fetal head employing the reverse breech maneuver. The mean age of women was 26.9±3.2 years, all at term between 38+5 and 41+6 weeks of gestation. The mean gravidity and parity was 2.1±1.7 and 1.1±1.7, respectively. The mean fetal weight was 3,540±474gm. and the mean time of full cervical dilatation was 106±53 minutes. All CS were performed in low transverse-incision. In two cases the incision had to be transformed to a J or inverted T shape. None of the cases had an inadvertent extension of the uterine incision. The mean estimated blood loss at CS was 580±100ml and the mean hemoglobin drop following operation was 1.8±0.7gm%. None of the women in the study needed a blood transfusion. The Apgar scores of newborns at 1’ and 5’ were 7.9±1.6 and 9.4±0.6, respectively. Umbilical cord PH was 7.27±0.05 and none had a PH lower than 7.15. As well, none of the newborns had a trauma related to the reverse breech extraction or were admitted to the neonatal ICU. All women following CS had uneventful postpartum period with no complications.

Conclusion: Our study shows that the reverse breech extraction is feasible in cases of second stage emergency CS with an impacted fetal head. Maternal as well as fetal complications following this maneuver seem to be low.
Objective: Should the cephalic-presenting, severely preterm fetus be allowed to deliver vaginally or be delivered by caesarean section? Recent studies purport to show improved survival or decreased morbidity for the neonate when caesarean delivery is performed for severe prematurity. This presentation will summarize the literature and make recommendations. This topic is extremely important for the health of women and infants worldwide.

Methods: A literature search was conducted to identify the available quality studies examining the relationship of delivery mode and survival for cephalic-presenting preterm fetuses. This is also performed for the studies addressing a decrease in morbidity from intracranial hemorrhage (ICH) and the clinical circumstance of fetal growth restriction (FGR). Studies are included in the summary only if regression analysis, the scientific method that attempts to control for confounding variables that may produce positive results in univariate analyses, was performed. Any extreme intervention (i.e., a surgical procedure such as caesarean delivery) is unlikely to be justified for many reasons. Additional analyses are performed for the difficulty in determining when delivery is imminent and the morbidity and mortality that may ensue for women when there is a policy of caesarean delivery for extreme prematurity.

Results: All of the available studies are retrospective in nature, limiting the quality of the information available. There have been attempts to perform randomized trials, of which several have failed. The highest quality scientific information is thus unavailable. The literature review shows mixed results. There are several studies that suggest that caesarean delivery is associated with improved survival of severely preterm fetuses, decreased morbidity from ICH or improved survival in the setting of FGR, while many others show no such associations. The most recent and largest studies, which far outweigh the others in numbers, also show mixed results for different gestational age or birth weight categories. The varying dynamics of preterm labor prevent an accurate prediction of imminent delivery, leading to the possibility that caesarean delivery may harm some fetuses that may have remained in utero for a much longer time. Cesarean delivery at an extremely preterm gestational age increases the risk of morbidity and mortality to the woman and her future fetuses, and these risks increase with each additional caesarean. These risks are due to placenta previa/accreta, major obstetric hemorrhage, uterine rupture, and peripartum hysterectomy in subsequent pregnancies.

Conclusions: Since no “gold-standard” scientific evidence exists for this topic (i.e., randomized trials), further study is necessary before setting any standard. These data do not provide enough scientific evidence to support a “blanket” recommendation for caesarean delivery as a method to improve survival for the cephalic-presenting, severely preterm fetus, to decrease the incidence of ICH in the severely preterm fetus, or to improve survival for the severely preterm fetus with FGR. The additional burden of morbidity and mortality in the index pregnancy and future pregnancies leads to the conclusion that a policy of caesarean delivery for the extremely premature fetus is not a viable option at the current time.
Intrauterine interventions in fetuses with critical aortic stenosis – analysis of 16 fetal aortic valvuloplasties

Wolfgang Arzt, Gerald Tulzer, Irene Veit, Dagmar Wertaschnigg, Roland Gitter

Linz, Austria

Introduction: Second trimester fetuses with critical aortic stenosis, dilated left ventricles with endocardial fibroelastosis and reverse aortic arch flow will have a postnatal univentricular circulation. To provide a postnatal biventricular circulation 16 intrauterine procedures have been done in Linz, Austria and success rate, risks and outcome were analyzed.

Methods:
Since December 2001 we have attempted 16 percutaneous ultrasound-guided aortic valvuloplasties in 15 fetuses (23+4 to 32+5 weeks). In 3 fetuses impaired right ventricular filling had resulted in advanced end-stage heart failure with hydrops.

Results: Aortic valvuloplasty was technically successful in 10/16 procedures (62.5%) or 10/15 fetuses (66.6%). Overall mortality was 3/16 (18.7%), in the last 14 procedures 1/14 (7.1%). Of the 5 fetuses with no technical success 2 died in-utero and 3 ended up as hypoplastic left heart syndrome. Of the 10 fetuses with technical success 7 patients now have a biventricular circulation after birth (1 is still in utero), 1 had a sudden IUD, 1 received a hybrid stage.
All of the 7 biventricular patients had to undergo another aortic valve dilatation in the first week of life, in 4 of them this was the only procedure so far with a follow-up of 1, 2, 24 and 29 months respectively.
All 3 fetuses with hydrops had a successful procedure and hydrops resolved within 3-5 weeks.

Conclusions: In selected fetuses with critical aortic stenosis in-utero valvuloplasty has the potential to save the left ventricle for a biventricular circulation after birth and to reverse end-stage heart failure with hydrops.
Prenatal treatment of fetal chest lesions (hydrothorax, CCAM, pulmonary sequestration)

Dick Oepkes

Leiden, Netherlands

Fetal hydrothorax is a rare but serious condition, easily recognized on ultrasound examination. Accumulation of fluid in the pleural space may lead to pulmonary hypoplasia, compression of the heart and obstruction of venous return with subsequent development of hydrops and compression of the esophagus leading to polyhydramnios. Untreated, the reported perinatal mortality is 22% to 53%. Systematic review of the literature on isolated hydrothorax suggests that both multiple thoracocenteses and thoraco-amniotic shunting are associated with perinatal survival rates around 65%.

Congenital cystic adenomatoid malformation (CCAM) may impair fetal swallowing, cardiac function and venous return, leading to polyhydramnios and nonimmune fetal hydrops. Untreated, perinatal mortality is over 80%. CCAM exists in a macrocystic and a microcystic variety. For solid-appearing lesions, drainage does not seem to be an option. Open fetal surgery via hysterotomy has resulted in a 29-65% perinatal survival rate. This procedure necessitates delivery by caesarean section. Thoraco-amniotic shunting for macrocystic CCAM, also for multilocular tumors, has resulted in high survival rates, with term vaginal deliveries and minimal maternal morbidity, as compared to open fetal surgery. We suggest that thoraco-amniotic shunting should always be considered prior to open fetal surgery for larger unilocular or multilocular macrocystic CCAM lesions presenting in association with fetal hydrops and/or polyhydramnios.

Large pulmonary sequestration with hydrops can be successfully treated by ultrasound guided minimally invasive laser surgery. It is therefore important to apply color Doppler for identification of a systemic feeding blood vessel in solid fetal lung tumors.
Major events in the history of perinatal medicine

Erich Saling

Berlin, Germany

Perinatal Medicine began to exist when also the fetus became accessible for applied medicine by a direct approach. This was achieved by analyzing its blood samples in 1960, published 1961. First there were serological and hematological examinations followed by blood gas and acid base analysis. The fetus became for the first time a real patient and obstetrics developed an essentially new character. As a physical community Perinatal Medicine exists since 1967 when the very first society in this field was officially founded. A much longer history exists for indirect approaches to the fetus. The most important concerns fetal heart rate diagnostics: 1818 first report on fetal heart sounds by Mayor; first graphic records of fetal heart actions in 1891 by Pestalozzi and in 1908 by Hofbauer & Weiss. In 1906 Cremer registered the first fetal electrocardiogram and in 1958 Caldeyro-Barcia the first heart rate record in combination with uterine contractions. This was the initial step for modern heart rate monitoring. But actual cardiotocography did not start until 1966 when Hammacher designed a suitable recording system, which became available for routine use in 1968. Amniotic cavity accesses: 1881 first amniocentesis by Lambl; 1930 first amniography by Meness; in 1952 Bevis used amniocentesis for diagnosing Rh– Erythroblastosis; 1961 spectrophotometric analysis of amniotic fluid and 1963 symptomatic treatment of severe fetal Rh-disease by Liley. We introduced amnioscopy in 1962 to assess increased fetal risk in late pregnancy. In 1967 we created the term "Perinatal Medicine" and, in view of all this new progress, recommended a reform of clinical structures which later have been established in the USA as "Maternal Fetal Units" in 1972.
Lessons from the past, thoughts for the future or the good, the bad and the villain…

Manuel Carrapato

St Maria da Feira, Portugal

Over 30 years ago the concept of Perinatal Medicine emerged - maternal deaths became almost an incident and, often, an accident; early neonatal and infant mortality have, similarly, been almost confined to the “inevitable” case. This is GOOD news.

In recent years an increased survival of even the most immature infants, often at the threshold of viability, has been reported. This is GOOD news.

Not so good, is that only 7% of all births happen in the western world, the remaining happening in developing countries. Of the 7 million perinatal deaths per year 98% occur in those countries. Each year ½ million women die from pregnancy related complications and including unsafe abortions – once again 99% of these maternal deaths are in the same unfortunate countries.

The sad thing is that most of these deaths are preventable!!! This is BAD news.

Pre-implantation genetic diagnosis (PGD) was developed for the early detection of genetic disorders, identifies chromosomal abnormalities and some monogenic illnesses, with potential for other disorders. PGD of sex-linked diseases and HLA typing for compatible stem sells donation after birth are acceptable. This is GOOD news. PGD for sex-selection without medical reasons, for embryo research or to enhance “desirable” traits might lead to VILLANY…

Cord blood transplantation has been used for various disorders, from malignant and non-malignant haematological disease, congenital immunodeficiencies and solid tumours. This is the GOOD news. However, cord blood banking may lead to questions of confidentiality, privacy and discloser or, even, the identification of diseases for which no cure exists. And this may lead to VILLANY…

Over the last thirty years of Perinatal Medicine and Care we have seen many of the GOOD deeds, some of the BAD and reckless attitudes and a fair amount of potential VILLANY. Hopefully, these lessons from the past will guide us into the future!
Quality of life will be more important than survival in very immature babies

Malcolm Levene

Leeds, UK

There has been a progressive increase in survival amongst the most immature babies in recent years but it now appears that survival statistics for those born on the edge of viability (23 weeks of gestation) are resistant to further improvement and in addition there appears to be a high risk of severely adverse neurodevelopmental outcome in survivors at 23 and 24 weeks of gestation. There is no evidence that this has improved in the last 10 years. The risk of death or severe disability in babies born at 23 weeks and 24 weeks is in the order of 90% and 75% respectively. The causes of disability in this very immature group are various and often not obvious. They may include cerebral ischaemia/haemorrhage, hypoxia/hyperoxia, nutritional deprivation, lack of appropriate micronutrient availability, hormonal imbalance or hypoglycaemia. Some of these can be recognized early in neonatal life by brain imaging but the majority are not apparent. Lesions evident on early scanning may allow appropriate discussion with parents and possible withdrawal of care.

The cost of neonatal intensive care in developing countries is increasing, but this cost is minor compared with that of life-long care for highly dependent disabled children and adults who survive extreme prematurely with severe brain damage. Health care systems are poor at providing long-term care particularly into adult life. In future health care systems will have to determine whether it is cost-effective or ethically appropriate to offer intensive care to babies with such a poor prognosis. This is both a medical problem to be considered by perinatologists but also a societal issue which must be discussed widely in the community in light of available resources for severely damaged children and adults.
Invited Speaker

Parallel session 5: Pre- and postnatal steroids

Postnatal steroids

Henry L. Halliday

Belfast, UK

Objective: To determine the role of postnatal steroids for prevention and treatment of chronic lung disease (CLD) or bronchopulmonary dysplasia in preterm infants.

Methods: The Results of randomized controlled trials (RCTs) and systematic reviews of RCTs were used to develop evidence-based guidelines for postnatal steroid therapy in preterm infants at risk of developing CLD.

Results: Two recent systematic reviews in the Cochrane Library show that postnatal steroids given either early (<7 days) or late (>7 days) reduce the risk of CLD at 36 weeks (RR 0.70; 95%CI 0.61-0.81 and 0.72; 0.61-0.85 respectively). These reductions in CLD translate into numbers need to treat (NNT) of 12 and 6 respectively. However, there are adverse neurological effects as cerebral palsy is significantly increased with early treatment (RR 1.75; 95%CI 1.20-2.55) but not late (1.22; 0.84-1.77). For early treatment the number needed to harm (NNH) is 15 (95%CI 8-57). Meta-regression including more than 4000 preterm infants in these RCTs shows that risk of developing cerebral palsy is inversely related to risk of developing CLD. Therefore use of steroids in babies at low risk of developing CLD will increase risk of later cerebral palsy. It also explains why risk of cerebral palsy is increased only in preterm infants treated early and therefore at lower risk of developing BPD.

Conclusions: Postnatal steroids should be avoided in the first week of life and reserved for babies at high risk of developing CLD or those who already have it. When needed steroids should be prescribed in the lowest dose for the shortest possible duration. There is still a role for steroids in the neonatal period and further research is needed to refine precise indications for their use.
Mode of delivery and outcome of the extremely preterm infant

Eduardo Bancalari

Miami, USA

There is an increasing rate of elective caesarean sections among extremely preterm births in the US despite lack of consensus on the impact of the mode of delivery in this population. This is in part because several studies have suggested that caesarean section may convey an advantage in survival and other important outcomes such as CNS hemorrhage in the smallest infants. However, most of the available data comes from retrospective studies without proper controls for the multiple variables that can influence these outcomes.

The lower mortality associated with caesarean sections has mostly been observed for infants born before 27 weeks of gestation and in breech presentation. While infants born by C/S have less risk of low Apgar scores, their risk for respiratory morbidity seems to be increased. The available data on mortality and morbidity is not strong and conclusive enough to recommend routine elective caesarean section in extremely premature infants. The possible advantages for the infant must be considered in the context of the increased maternal morbidity induced by a caesarean section in early gestation.
Probiotics in preterm neonates

Paolo Manzoni

Torino, Italy

Background: Preterm neonates in NICU are highly at risk of intestinal disturbances with proliferation of a pathogenic microflora, because treatment with antibiotics, total parenteral nutrition, or nursing in incubators may delay or impair the intestinal colonization process. Preterms thus acquire commensals such as bifidobacteria more slowly and are likely to acquire gut pathogenic colonization from the NICU. For all these reasons, the digestive tract is regarded as the most important reservoir and site for colonization by all kinds of pathogens and subsequent sepsis in preterms. Probiotics can restore normality of gut microbiota, and prevent its disturbances in humans including neonates.

Studies in mice have shown that selected probiotic strains reduce both enteric colonization and systemic infections by E. Coli and fungi. Such strains may act at several levels simultaneously: exclusion of pathogens by competition, prevention of adhesion, reduction of their ability to colonise the mucosa through enhanced IgA responses, changes in mucosal permeability increasing the barrier effect, and immunomodulation with modification of local immune responses and of host response to fungal and bacterial toxins and products.

To date, only a few clinical trials have reported the outcomes of preterm neonates given probiotics: these studies consistently show beneficial effects of some probiotic mixtures in preventing fungal colonization, improving feeding tolerance, and reducing the incidence of necrotizing enterocolitis. In view of the beneficial effects of probiotics on gastrointestinal maturity and function, their administration to preterm infants in NICU is an area of current interest and of accumulating evidence. However, concerns exist about safety and tolerability of probiotics administered to preterm infants, as long-lasting administration of living microorganisms to immature patients might translate into breakthrough infections by these probiotics. This will be a major area of research in the future.
Outcome of extremely premature infants. Results of the EuroNeoStat project

Adolf Valls i Soler

Bilbao, Spain

Background: Very-low-gestational-age (VLGA) and birth-weight (VLBW) are the main factor related to perinatal, neonatal and infant mortality and morbidity throughout the world. The European Neonatal Network (EuroNeoNet) is supported by EuroNeoStat, a DG SANCO funded project.

Aim: To report the short- and long-term outcomes of VLGA infants born at the European Neonatal Units (NICUs) belonging to EuroNeoNet, and to stress the clinical variability encountered (NICUs with >5 infants/year).

Methods: VLGA infants born at 66 NICUs from 13 European counties are included in this study (n=4855). Perinatal risk and protective factors, neonatal interventions and complications as well as mortality and main morbidities are analyzed. The Results are reported by gestational age strata. Factors affecting mortality are analyzed, and a combined outcome for survival without significant morbidities is evaluated.

Results: Mean neonatal mortality rate of the cohort of infants studied was 14.3%, varying among NICUs from 1.8 to 40%. Factors affecting clinical variability will be outlined. Initial follow-up data of the historical cohort will also be presented.

Conclusions: There is clinical variability in the outcomes of VLGA infants cared at EuroNeoNet participating NICUs. Consensus on a minimal follow-up data set seems mandatory to be able to compare long-term outcomes of those very-high-risk infants.

We acknowledge DG SANCO for funded the EuroNeoStat project (Nº 116/2007)
Variation of organisation of care and medical practices for very preterm babies in Europe

Jennifer Zeitlin

Paris, France

Background: The organization of perinatal care affects the prognosis of very preterm babies. Being born in a perinatal centre combining a maternity unit and a neonatal intensive care unit (a level III unit) is associated with lower mortality and morbidity. Beyond this well accepted fact, however, it is unclear how health services should be organized for this population.

Methods: The “Models of organizing access to intensive care for very preterm births (MOSAIC)” study compared health outcomes and care in 10 European regions with different models of perinatal care by constituting a population-based cohort of 7222 babies in 2003. Data were also collected from maternity and neonatal units in participating regions to describe the structural characteristics.

Results: This study revealed large differences in health outcomes in the participating regions. We found that the 65 level III units included in MOSAIC were highly heterogeneous with respect to personnel, their volume of admissions and services provided. While we found that reduced access to specialized care increased mortality and morbidity everywhere, the association of health outcomes with other structural factors considered key by policy makers and clinicians, including unit size, personnel qualification and provision of specialized services, remained elusive. These associations were obscured by the difficulty of defining comparable measures of health care inputs and large regional and unit specific differences in medical practices, for instance in respiratory support and use of caesarean section.

Conclusions: Care provision for very preterm babies in Europe differs greatly between regions. New research strategies should be adopted to generate scientific evidence about the effectiveness of these varied approaches.
Uterine activity: Enough is enough

Petra Bakker

Amsterdam, The Netherlands

Uterine contractions cause decreased blood flow through the uterine artery. In the healthy uncompromised fetus, this will not end in fetal acidemia. The fetus has developed protection mechanisms to survive labor: (1) During a uterine contraction fetal preload increases and enables the fetus to maintain a constant blood flow through the umbilical artery and (2) uterine activity increases the blood flow in the fetal middle cerebral artery; i.e. the so-called brain-sparing effect. Shortcomings of these protection mechanisms in the compromised fetus and/or in case of excessive uterine activity increase the risk of adverse fetal outcome. The brain-sparing effect will become more pronounced to compensate for the decreased umbilical artery blood flow and the impaired fetal oxygenation. Maintenance of normal uterine activity, especially a sufficiently long relaxation time between contractions, is essential so that the supply of well oxygenated maternal blood to the intervillous space will be restored and the cerebral oxygen saturation can remain stable. Incorrect use of oxytocin can be very dangerous with regard of the condition of the fetus and is a frequent cause for litigation in medico-legal cases. Since special safeguards are required to reduce the risk of error, the Institute for Safe Medication Practices (ISMP) placed oxytocin on the high alert medication list. The implementation of a checklist protocol for the use of oxytocin is strongly recommended.
Cardiotocography plus ST-analysis of the fetal electrocardiogram versus cardiotocography only for intrapartum monitoring: A Dutch randomized trial

Anneke Kwee

Utrecht, NL

Background: Intrapartum surveillance with ST-analysis of the fetal electrocardiogram (ECG; STAN®) potentially improves neonatal outcome.

Methods: We performed a randomized trial among laboring women with a high-risk singleton pregnancy in cephalic position beyond 36 weeks of gestation. Participants were assigned to monitoring by cardiotocography (CTG) combined with ST-analysis (index) or CTG without ST-analysis (control). There were strict conditions for performance of a fetal blood sample (FBS). Primary outcome was metabolic acidosis defined as umbilical cord-artery pH below 7.05 combined with a base deficit calculated in the extracellular fluid compartment above 12mmol/L.

Results: We randomized 5681 women (2832 index; 2849 control). The FBS rate was 10.6% in the index group versus 20.4% in the control group (relative risk (RR) 0.52; 95% confidence interval [CI], 0.46 to 0.60). The incidence of the primary outcome was 0.7% in the index group versus 1.1% in the control group (RR 0.70; 95% CI 0.38 to 1.28). When metabolic acidosis was analyzed according to the base deficit calculated in blood, these rates were 1.6% and 2.6%, respectively (RR 0.63; 95% CI, 0.42 to 0.94). The number of operative deliveries, low Apgar scores, neonatal admissions and newborns with moderate or severe hypoxic ischemic encephalopathy (HIE) was comparable in both groups.

Conclusions: Addition of ST-analysis of the fetal ECG to surveillance with CTG during labor reduces the number of newborns with (metabolic) acidosis, without an effect on Apgar scores, neonatal admissions, moderate to severe HIE or operative deliveries.

(Trial Registration Number, ISRCTN95732366)
Full intrapartum surveillance by the centralized automated monitoring and warning system

Kazuo Maeda

Yonago, Tottoriken, Japan

Aims: As the neonatal asphyxia, perinatal mortality and cerebral palsy reduced after individual intrapartum CTG monitoring in our past experience, full FHR monitoring was expected to be promising by the centralized automated fetal monitoring in the large number of births' hospitals and in the time consuming individual monitoring. Methods: The multiple time sharing is carried out in the simultaneous monitoring, where the FHR data are transmitted by wireless telemetry, the decision is made on the quantified FHR data by the parallel programs of experts' knowledge and artificial neural network systems. The pathologic sinusoidal FHR is detected by the FHR frequency spectrum. False positive changes are excluded. Abnormal FHR changes, non-reassuring status, abnormal score, probability to be pathologic outcome, pathologic sinusoidal FHR and the CTG etc., are automatically displayed on the physicians' cellular phones. The CTG is not recorded but printed as the hard copy on demand, and original data are stored in the computer memory. TOITU (Tokyo) produced the system according to the author's plans. Results: Mild to severe neonatal asphyxia is predicted by the FHR score even in the 1st stage of labor, which correlated fetal scalp blood pH in the 2nd stage. The probability to be pathologic outcome calculated by the neural network system coincided with the FHR score, the neural index predicted the outcome of prolonged labor and UApH. The system will be capable to monitor more than 10,000 births in a year. Conclusion: Full intrapartum surveillance is accomplished by the centralized fetal monitoring and warning system.
Sinusoidal-like patterns: What do they mean?

Jan G. Nijhuis

Maastricht, NL

The interpretation of cardiotocography tracings (CTG) is still crucial in modern technology, both during pregnancy and labor. “Eye-balling” the pattern is important, but a structured analysis should always be performed. One starts with the judgment of contractions and/or hypertonia, then the baseline, variability, accelerations, and decelerations, followed by a conclusion. A thorough description helps to be more precise and accurate. In some cases a sinusoidal-like pattern (SLP) can be noticed. Classically, a sinusoidal CTG has been associated with severe fetal anemia. This is certainly still valid, but similar patterns can also occur under different circumstances. The point is not the precise definition of a sinus, but rather the observation or recognition of a possible sinus: when a SLP is observed, one should not jump to conclusions, but rather make a differential diagnosis and try and find the reason for this pattern. Normal fetal behavior may elicit a SLP as well: fetal regular mouthing “movements” during state 1F (“non-REM-sleep”) leads to a small sinus pattern, while fetal sucking movements in state 3F (“quiet awake”) may lead to a SLP with a much larger sinus. Also, drugs like pethidine and meperidine may evoke a SHP, and the use of medication should therefore be considered.

Finally, even if the maternal heart rate is recorded, and not the fetus (!), a SLP can be seen, especially during the second stage of labor.

In conclusion, when one observes a SLP, one should always work on the differential diagnosis, and continue the recording. The sudden appearance of a SLP is seldom worrisome, and in most cases there is time to think, before unnecessary interventions are undertaken.
STAN – experience earned from 500000 deliveries

Karl G. Rosen

Gothenburg, Sweden

An important aspect of health care developments is to conduct quality improvement research to allow the assessment of quality of care in a total population beyond what is possible with randomized clinical trials. The largest cohort of term deliveries so far studied originates from a 7-year prospective study of 22171 deliveries (2001 – 2007) from Moelndal District Hospital (H. Norén and A. Carlsson). Four yearly cohorts of 12832 term pregnancies were part of a detailed analysis.

Results The STAN usage rate increased from 26 to 69%. The cord metabolic acidosis rate was reduced from 0.72 to 0.06%. This 91.7% improvement was associated with a significant reduction in the number of cases with a prolonged response time, calculated as the time from CTG+ST indications to intervene until delivery and an ability of the staff to identify and act upon preterminal and unstable FHR patterns at onset of a recording. Only one case with metabolic acidosis and neonatal seizures (shoulder dystocia with subarachnoidal bleeding in connection with a complicated vacuum extraction) was born during the last 18 months of the study period including 5228 term deliveries in active labor.

Conclusions: These quality improvement data indicate a paradigm shift in the outcome of delivery related to a high rate of CTG+ST usage and the application of structured CTG analysis. To achieve a paradigm shift from screening to diagnostic capacity requires not only new knowledge and new technology, equally important is the readiness to adhere to new guidelines and thereby assuming responsibility for our future.
Appraising maternal & fetal well-being in labor: Midwifery practices

Holly Kennedy

San Francisco, USA

Evidence supports that most women who are healthy entering parturition have the requisite capacity to birth their infants proficiently and with little intervention. However, maternity practices often do not reflect or draw upon the strengths of women’s ability to birth, but focus on the potential risk. This is sometimes called the 1% doctrine where interventive surveillance techniques are applied to most women in hope of preventing problems for the small minority who will develop them. There is growing concern that these practices may be causing more harm than good, both short-term and long-term. Is it possible to reverse this trend? A recent Cochrane review of midwifery-led care supports a model of care that is markedly less interventive. This paper will discuss the following issues of caring for women during labor and birth, in particular as they relate to surveillance practices: 1) evidence that supports the health effects of personalized, and woman-centered care; 2) the interplay of physiologic and psychosocial factors; 3) the role of pain and its difference from suffering; 4) specific surveillance practices commonly applied by midwives; and 5) the skill of patient, careful observation. It will conclude with a critical examination of the state of maternity care as practiced in many developed countries and a thoughtful discussion of future directions and call for future research.
The topic of pelvic floor assessment is increasingly attracting attention. This is not surprising- after all, many women who have given birth naturally are affected by pelvic floor trauma, and so are their partners. Health professionals deal with the eventual consequences of such trauma, especially pelvic organ prolapse and fecal incontinence. Until recently ‘pelvic floor trauma’ meant perineal and vaginal tears, and damage to the anal sphincter. In developing countries especially, pelvic floor trauma also includes fistulae, but these are uncommon in developed countries with good intrapartum care. Anal sphincter trauma has received much attention over the last 20 years and will not be dealt with here. We now know that ‘pelvic floor trauma’ encompasses more than what we’ve been taught to identify and repair in delivery suite. In 15-30% of all women there is serious damage to the puborectalis component of the levator ani muscle after vaginal delivery. This trauma commonly affects the insertion of the puborectalis muscle on the inferior pubic ramus and has been termed an ‘avulsion’ injury. It is associated with vaginal operative delivery, especially Forceps, and with higher age at first delivery. An avulsion reduces contraction strength by about 1/3 and increases dimensions and distensibility of the levator hiatus. It markedly increases the risk of anterior and central compartment prolapse, and it seems to be a risk factor for prolapse recurrence after surgical repair. Diagnosis is possible by palpation and ultrasound or MR, with the latter method the least practical. First attempts at primary and secondary repair have been unsuccessful, and prelabor prediction seems difficult. Several prevention trials are in planning or in progress. This presentation will give an overview of the current state of research in this field and develop perspectives for the future.
ITU (Infrapubic translabial ultrasound)

Wolfgang Henrich

Berlin, Germany

Infrapubic translabial ultrasound in the second stage of labor has been recently been suggested to improve the ability to assess fetal head station and position. Dietz et al. proposed the use of a translabial approach and suggested calculation of the distance between the pubis and the lowest edge of the fetal head to evaluate engagement. We observed that descent of the fetal head during second stage of labor followed a curvilinear path. In a sagittal plane, the head was progressively directed downward, horizontally and eventually upward. Using a 3D CT reconstruction of maternal pelvis we also demonstrated that the ischial spine level is usually 3cm below the pubic bone which allows for a more precise evaluation of the fetal station. We also reported that the upward direction of the fetal head is highly predictive of imminent vaginal delivery or easy vacuum extraction, particularly if upward movement was sonographically observed during patient pushing. Using volume reconstruction, we could demonstrate internal rotation of the fetal head by surface rendering of the fetal skull. Most of the experience reported in the literature so far has been obtained with standard two-dimensional ultrasound.

In collaboration with GE Healthcare a dedicated software to evaluate fetal position by using three dimensional (3D) ultrasound technologies (Sonography-Based Volume Computer Aided Display SonoVCAD™ labor) was implemented. Offline analysis of ultrasound volumes allows a more accurate alignment of anatomic landmarks of maternal and fetal structures and, by aligning and comparing serial volumes, of the progression of the fetal head. In the sagittal plane, head progression, head direction and angle of descent can be conveniently measured using the software. Switching from the sagittal to the axial plane allows for calculation of the midline angle (defined as the angle between the anterior-posterior axis of maternal pelvis and the head midline).
Intrapartum translabial ultrasound (ITU): Comparison of parameters and analysis of birth mechanics

Boris Tutschek

Bern, Switzerland

Introduction
Intrapartum translabial ultrasound (ITU) enables objective non-invasive assessment of labour in cephalic presentation singleton births. Qualitative and quantitative parameters have been described (Henrich et al. 2005, Barbera et al. 2009, Ghi et al. 2009). In a sagittal view descent on pushing, widest diameter of the fetal head below certain landmarks (i.e. head station) and, with regard to the long axis of the pubic bone, direction of the head and the angle between the symphysis and the tangent of the fetal skull have been used. In a transverse view the angle of the midline echo shows head rotation. The descending head’s dynamics during voluntary pushing have not been studied.

Objective
To measure and compare different quantitative parameters of ITU during voluntary pushing in normal labour and to analyze normal fetal head descent.

Patients and methods
50 healthy pregnant women with singleton gestations in cephalic presentation during spontaneous term labour were studied with ITU and manual palpation.
Intra- and inter-observer repeatability XY plots (with lines of equality) according to Bland Altman were used to assess repeatability. Normal head descent at stations above and below the 0 station was analyzed semi-graphically.

Results
Intra- and inter-observer variabilities for ITU head station, head direction and angle of descent were +1cm, +16° and +8° and 1.6cm, 16° and 14°, respectively.
In occiput-anterior presentation, the fetal head travels parallel to the pubic bone in the upper two thirds, and descent is greater during voluntary pushing. Then, rotation occurs; there is less descent and more change in head direction. Rotation obscures visual and quantitative assessment from sagittal ITU. Occiput-posterior heads follow a different pattern.

Conclusion
Repeatability was sufficient for all parameters. Different effects of voluntary pushing can be observed depending on true head station. Head rotation should also be assessed using a transverse ITU insonation. Fetal heads in occiput-posterior cephalic presentation have a different sequence of descent-related changes.
A framework for ethical decision making in neonatal intensive care

Hans Ulrich Bucher

Zürich, Switzerland

At our NICU we analysed the status quo of decision-making about withdrawing or withholding intensive care in neonates and concluded that neither decisions by the head of the unit or the most experienced senior doctor, nor strict adherence to national guidelines, nor delegation to the parents or to an ethical committee were satisfactory.

We therefore developed a framework for structured decision making and demonstrated its impact on health care and on survival of critically ill neonates.

This discussion group is structured into an “inner circle” and an “outer circle”. The “inner circle” consists of nurses and doctors who are directly involved in the care of the infant. Only they are responsible for the final decision. The “outer circle” consists of medical experts (neurologists, cardiologists, surgeons, etc.), other staff members, medical students and members of the Neonatal Ethics Group. The discussion is led by an independent moderator who is not involved in the care of the infant. He or she is responsible for maintaining the structure of the discussion. Parents do not participate in the discussion round but their way of life and their value system are taken absolutely seriously. They are informed about the proposition of the “inner circle” by the doctor and nurses who have the closest relationship with them and they have to agree.

An external evaluation of 84 sessions over three years revealed a beneficial effect on the quality of the decision making process itself and on the quality of the teamwork in the unit – especially the cooperation between nurses and doctors. Survival time in dying patients was shortened from 2 to 7 days.

Conclusion: The introduction of this framework for structured decision making involving doctors and nurses improved the quality of the teamwork. It shortened futile intensive care, and thereby suffering for both infants and parents.
Is feticide justified?

Joseph G. Schenker

Jerusalem, Israel

Perinatologists face difficult decisions about viable fetus feticide, late-term abortion; they confront limits that ethics and the law impose. Viability is a function of both fetal development and available biomedical technology and skilled personnel to use that technology to supplant immature fetal physiology after premature live birth. Feticide should be performing for all terminations at gestational age of more than 21 weeks and 6 days; the method chosen should ensure that the fetus is born dead. There are several reported methods, the intra cardiac potassium chloride is the recommended method and the dose should ensure that fetal asystole has been achieved. There are two main ethical views regarding the status of the fetus, the one is that the fetus is categorically denied independent moral status. The opposite view supported by the right-to-life movement, holds that the fetus categorically has independent moral status. The law in some nations, such as Israel, for example, specifically excludes the fetus as a person, and therefore there is not of gestational age for termination of pregnancy according to the Act of Abortion 1977. The main indication for feticide is fetal abnormalities. With increasing technology for screening and diagnostic testing for fetal abnormality in pregnancy, many more pregnant women and couples are faced with the decision to terminate a pregnancy often after receiving diagnostic test Results in the second or third trimester of pregnancy.

However, some severe abnormalities are not detectable until gestational ages close to or beyond the threshold of viability for independent life and in those cases feticide should be consider. The first includes instances when it is not in the fetus’s own best interest to live. Second, one must consider instances of fetal anomaly which may not be so severe as to preclude life, but sufficiently severe to cause hardship to interested such third parties as parents, siblings or society at large.

The medical, legal ethical and social aspects will be discussed.
Effects of IVF on imprinted disorders

Øjvind Lidegaard

Copenhagen, Denmark

While the majority of genes are silenced during differentiation leaving few active genes to ensure the specific function of a particular cell, few gene alleles are differentially blocked, so that the gene in one allele is blocked while the other remains active. This differential blocking of the same gene in two alleles is called imprinting. Imprinting disorders occur when the epigenetic programming during gametogenesis is disturbed, or when this programming is not sufficiently sustained during the process of fertilization and early embryonic development. Several case or case-reference reports have been published suggesting that compared with reference populations, a higher proportion of children with imprinting diseases were conceived by assisted reproductive technologies (ART). These reports are inconsistent in linking the risk to a specific assisted reproductive technology, and a cytogenetic examination assessing the exact genetic imprinting mechanism is often missing. Two national systematic follow-up studies on 6052 Danish and 16280 Swedish ART-children found none and two children with imprinting diseases, respectively. These figures correspond approximately to the expected number of children with imprinting disease from the general population.

In conclusion, we have only little evidence of an increased risk of imprinting diseases in ART children, but long-term multinational follow-up studies are warranted. Imprinting will in the next decade probably be one of the main focuses of reproductive research, as many diseases may be influenced by epigenetic programming during gametogenesis, and perhaps also in early embryonic life. Could be that the key mechanism of the so-called Barker hypothesis may be mediated through just epigenetic programming. Combined epidemiological and biomedical research will probably bring much new insight in the next decade.
In addition to the increase in adult and childhood obesity, there has been a significant increase in birth weight in developed countries over the last 20 years. Maternal pregravid obesity and glucose intolerance appear to be the strongest risk factors. The increase in birth weight most likely represents an increase in fat mass rather than lean mass. In addition to increased adipose tissue, neonates of obese women have increased insulin resistance as compared with the infants of average weight women. Prospective longitudinal studies have correlated maternal obesity and glucose intolerance as significant risk factors for childhood obesity and metabolic dysregulation.

What are the potential mechanisms related to increased fetal growth/adiposity in obese and glucose intolerant women? Although maternal weight gain is strongly correlated with fetal growth in lean women, maternal weight gain during pregnancy in overweight/obese women is actually less than that observed in lean/average weight women. Although almost 2/3 of fetal growth, including accretion of almost all of the adipose tissue, occurs in the last third of pregnancy, factors in early gestation, such as maternal pre-gravid obesity and glucose control, have the strongest correlation with fetal growth at term.

Based on these observations our group has been evaluating the interaction of the maternal metabolic environment in early gestation and effect on placental growth and function. Our recent data suggest that the chronic state of mild inflammation, pre-existing pregnancy in obese women, triggers the expression of immune-related genes at early developmental stages of the feto-placenta unit. Altered placental function is associated with a selective increase in transport and mobilization of maternal lipid substrates, for the fetus. If prevention of obesity is the goal rather than treatment then strategies addressing maternal pre-gravid obesity assume importance not only for the women but for her offspring as well.
Fetal growth and long-term outcome: Role of fetal and neonatal overfeeding

Andreas Plagemann

Berlin, Germany

Health and diseases are generally perceived to be caused genetically. It is meanwhile accepted, however, that alterations of the intrauterine and early postnatal nutritional, metabolic, and hormonal environment may also predispose for disorders and diseases throughout life. Pathophysiological mechanisms responsible for perinatally acquired 'malprogramming' are still unclear.

Gestational diabetes (GD) is characterized by fetal glucose overfeeding leading to fetal hyperinsulinism, which typically Results in macrosomia at birth. Similar may occur through maternal overweight, maternal overnutrition and increased maternal weight gain during pregnancy. Notably, in parallel with the general 'diabesity' epidemics, GD and overweight in pregnant women meanwhile reach dramatic prevalences while simultaneously mean birth weight and frequencies of 'fat babies' rise. Overweight at birth, however, predisposes to overweight in later life leading to an epigenetic vicious circle of 'diabesity' over succeeding generations of the maternal line.

Moreover, also rapid weight gain in neonatal and infant life is associated with later obesity risk, probably induced by causative neonatal overfeeding. Interestingly, breastfeeding as compared to formula has been shown to effectively decrease offspring obesity risk for the long term. Experimental data indicate that fetal and neonatal overfeeding may lead to hormonally induced, epigenetic malprogramming of key regulatory systems of body weight and metabolism, resulting in permanent obesity disposition.

Therefore, universal screening and respective therapy of all types of diabetes during pregnancy, avoidance of maternal overweight and overnutrition during pregnancy as well as avoidance of neonatal and infant overfeeding may be effective approaches for a primary perinatal prevention of 'diabesity' for the long term.

Fetal growth and fetal programming

André Van Assche

Leuven, Belgium

There is major evidence that abnormal fetal growth has consequences in later life. Fetal overgrowth (macrosomia) is related to hyperplasia of the insulin producing B cells and hyperinsulinism. It may be suggested that these (over) stimulation of the B cells during intrauterine life may lead to a reduced capacity for insulin secretion; certainly in conditions of an increased demand for insulin secretion such as pregnancy and obesity. These both conditions are characterized by insulin resistance. Intra-uterine growth restriction is related to hypoplasia of the insulin producing B cells and hypoinsulinism. Underdevelopment of the pancreatic B cells during intra-uterine life may also induce decreased adaptation of B cell function in later life. There are also suggestions that insulin resistance in adult life may be the consequence of reduced triggering of the insulin receptor function in utero.

The classical example of fetal macrosomia is the result of maternal diabetes, however there is increasing interest in developmental programming related to obesity. Obesity is becoming an epidemic problem not only in the developed, but also in the underdeveloped world. Maternal obesity is not only a risk factor for maternal and fetal outcome. Maternal obesity increases also the risk of obesity and insulin resistance in the offspring. Fetal growth depends on many factors; furthermore the working mechanisms of developmental programming are not yet fully understood.

In our presentation we will show human data and experimental data in the rat on fetal development and long-term consequences.
Micronutrients in the periconceptional period

Renate Bergmann

Berlin, Germany

The nutritional status of women in the periconceptional period is not only important for the health of the mother, it is also a resource for the fetal nutrient supply. Micronutrient deficiency of women can occur in both states, in undernutrition and in overnutrition, sometimes as hidden hunger. In humans, inadequate intake of single nutrients usually does not occur in isolation. But for some micronutrients effects have been demonstrated with consistency. An adequate perinatal supply of folic acid during the first 8 weeks of pregnancy protects against neural tube defects (NTD). Women of childbearing age that may become pregnant, and during at least the first two months of pregnancy, should aim at reaching an added intake of 400 µg/day of folic acid. To prevent recurrence of NTD 4mg/day should be taken. Low iodine stores can alter growth and impair development of the fetus. Although salt iodization has been implemented in many countries, a supplement containing 100 µg/day iodine is recommended in Europe before and during pregnancy. Iron deficiency in pregnancy increases the risk for maternal morbidity and mortality, premature birth, low birth weight and stillbirth. Low or empty iron stores (Ferritin <30µg/l) before pregnancy should be replenished by iron supplements (30-40mg/day). Vitamin A is required for a normal embryonic development. High doses (>3000 µg/day preformed vitamin A) in early pregnancy may be teratogenic and should be avoided. A low Vitamin B12 status, which is prevalent in vegetarians, increases the risk of abortions, preeclampsia and preterm delivery. Zinc deficiency, which is common in undernutrition and with parasitic infections, may cause malformations. To avoid micronutrient deficiency in the periconceptional period information and education can motivate to practice a healthy lifestyle and diet, benefits are expected from food fortification programs, and supplements containing micronutrients at adequate dosages should be implemented timely.
Periconception care

Amos Grunebaum

New York, USA

The traditional first prenatal visit is often too late to affect many adverse reproductive outcomes especially those associated with abnormal organogenesis secondary to drugs, alcohol, and poor diet. Pregnancy outcomes can be positively affected not only during pregnancy but also through preconception care.

Periconception care is the promotion of the health and well-being of a woman, her partner, and the baby before pregnancy. The goal of a preconception visit is to identify medical and social conditions that may put the mother or fetus at risk and to then implement changes which will improve pregnancy outcomes.

Key elements of preconceptual care include:
1. Screening for certain infectious diseases as STDs such as HIV, hepatitis B, Chlamydia, gonorrhea, and updating immunizations.
2. Obtaining genetic history and appropriate testing and counseling. The woman’s family history and ethnicity for genetic disorders (such as cystic fibrosis, sickle cell anemia, and Tay-Sachs disease) and malformations (such as neural tube defects) should be reviewed.
3. Identify medications and chemicals that are potentially teratogenic before conception and discourage their use during preconception and early pregnancy periods. Educate about smoking and alcohol and emphasize regular exercise and talk about adverse effects of certain foods.
4. Providing specific nutritional advice and ensure optimal weight. This specifically includes taking a prenatal vitamin supplement include 600 mcg folic acid daily.
5. Review fertility issues and educate the couple about optimizing fertility. Perform tests if fertility may be an issue.
Genetic counseling: Its role in the preconceptional care

Zoltán Papp

Budapest, Hungary

Genetic counseling is a communication process concerning the occurrence and the risk of recurrence of genetic disorders within a family. The aim of such counseling is to provide the counselee(s) with as complete an understanding of the disorder and/or problem as possible and of all the options. The counseling process is also aimed at helping families cope with their problems and at assisting and supporting them in their decision making.

Expectations at the first preconception visit at the genetic counseling service include routine documentation of the medical, obstetric, and genetic history, including construction of a family pedigree. The indications for preconception genetic counseling should be determined at the first visit and can be considered in a few clear categories:

- advanced maternal age
- a previous fetus or child with a genetic disorder
- a parent with a genetic disorder
- genetic disorders that pregnancy may aggravate
- maternal genetic disorders that may threaten fetal health and survival
- a history of infertility
- parental carrier of a genetic disorder
- family history of a genetic disorder
- consanguinity
- environmental exposures that threaten fetal health

Preconception counseling identifies specific risks and attendant options, which include:

- decision not to have children (includes consideration of vasectomy or tubal ligation)
- adoption
- in vitro fertilization and other reproductive technologies
- carrier detection tests
- presymptomatic and predictive testing
- preimplantation genetic diagnosis
- folic acid supplementation in periconceptional period.

The optimal time to initiate counseling is not during pregnancy. Counselees whose first antenatal visits occur after the second missed menstrual period miss the critical period of organogenesis, and patients referred well after conception have lost almost all their options except selective abortion.
Preconceptional care

Eric A. P. Steegers

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Over the last few decades, reproductive health has not improved and the impact of lifestyle related risks has become increasingly clear. The numbers of children born preterm, growth restricted or with congenital abnormalities have not diminished. In the United States maternal mortality has shown only a modest decrease in the last decades whilst in The Netherlands it has even increased. Preconception care is important for optimal intrauterine growth and development as it is the only way by which appropriate action can be taken in time with regard to early placentation and successful embryogenesis. The principal goals of preconception care are to optimize the health of the future child and to improve maternal health through primary intervention. General preconception care entails risk assessment, health promotion, counseling and intervention. Risk assessment is the systematic identification and evaluation of risk factors for so-called adverse pregnancy outcome. If risks appear, this may require additional screening, diagnostic tests and consultation of specialists. Health promotion consists of informing and educating couples on a variety of health-promotion issues and measures, including periconceptional folic acid supplementation, avoidance of alcohol, tobacco and other drugs, and the importance of proper nutrition. Intervention is carried out in order to modify or eliminate risk factors. Counseling allows people to make an informed choice on whether to opt for pregnancy (and how) or not to opt for pregnancy. Specialized preconception care is offered to women at increased risk of an adverse pregnancy outcome, like women with a complicated medical, obstetrical or family history, chronic diseases and conditions like congenital cardiac defects as well as previous organ transplantation. Preconception care can be seen as a window of opportunity to improve children’s health, women’s health and public health at the same time.
Cancer and pregnancy – obstetrical view

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The frequency of diagnosed malignancies is overall the same in pregnant versus non-pregnant women of the same age. However, in the industrialized world, we are experiencing an increase in the incidence of malignant diseases in pregnancy. This increase is attributable to demographic developments bringing changes in childbearing behavior and increasing numbers of older pregnant women. Looking ahead, this trend foreshadows ongoing growth in the coincidence of neoplasia and pregnancy.

Given this trend, we have to acknowledge that specifically and especially in pregnancy the level of knowledge on the course and prognosis of malignant diseases is low. Our therapeutic decisions are mostly based only on case reports and retrospective studies. Representative data on fetal outcome in neoplasia and pregnancy is usually missing, as is data on the complications of cancer treatment during pregnancy, the consequences of this treatment for the neonate, and its impact on long-term development.

When we counsel a pregnant woman with a malignant disease, not only have the pregnancy and the child to be considered, but also the influence of the malignancy on the pregnancy and, on the other hand, the influence which the pregnancy has on the malignant disease. It seems that our current knowledge can be summarized as follows: The tumor biology of malignancies is not changed by the pregnancy, and the disease prognosis depends on stage-related therapy.

The diagnosis and the therapy of malignancies in pregnancy are necessarily interdisciplinary challenges. From the obstetrical perspective, two aspects should be considered equally: The consequences for prematurity, and the effects of adjuvant and surgical procedures on the fetus and the pregnant woman.
Effect of conservative cervical surgery on pregnancy outcome

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There is now a considerable published literature of observational studies reporting an association between cervical surgery and increased risk of preterm birth. This accumulated evidence is supportive of a causal relationship despite the uncertainty that confounding due to unknown or poorly measured shared risk factors for CIN and preterm birth could explain the observed increase in risk. Large linkage studies from Scandinavia have demonstrated that the increased risk of preterm birth occurs at all gestations and the increase in risk remains, although attenuated, when a control group of women giving birth prior to cervical treatment is used. Cold knife cone and LLETZ/LEEP are consistently associated with increased risk and ablative therapies generally not associated with increased risk. The absence of risk associated with ablative therapies is further evidence that the association with excisional therapies is causal. Data supporting a dose response relationship between height of cone and risk of preterm birth are also accumulating.

The importance of this research includes providing evidence to support studies of conservative approaches to cervical screening (such as delaying to age 25), development of more specific screening tests, evaluation of delaying referral and intervention for low grade abnormalities in young women, and natural history studies of the rates of regression or progression of HPV related disease. In many countries, “see and treat” protocols are no longer recommended. Few studies have explored the mechanisms mediating the effects of cervical treatments on pregnancy outcome. This should be a focus for future research and has the potential to elucidate the pathophysiological mechanisms of preterm birth.
Cervical cancer in pregnancy

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Berlin, Germany

In recent years, an elevated incidence of cancer during gestation has been detected, probably related to the tendency of increasing maternal age. Cervical cancer (CC) classically occurs in young patients, with a median age of 45 years and is considered the most common cancer associated with pregnancy. The estimated incidence is approximately 1 per 200 to 10000 pregnancies, depending on whether pre-cancer is included. In parallel, a significant decrease of parity has changed completely the maternal profile. Thus, when cervical cancer complicates gestation, this pregnancy may represent the only opportunity of the patient to become a mother.

Cervical cancer in pregnancy is a challenge for the patient, her family and the medical staff. In the past, for a diagnosis before 20 weeks of gestation, the standard management was termination of pregnancy in order to not delay cancer treatment. However, recent studies attesting the safety of cancer treatment delay to reach fetal viability and the fact that gestation does not seem to have a negative impact on oncologic prognosis have changed this concept. Although CC treatment guidelines for non-gravid patients are well defined based on several randomized trials, there is a noticeable absence of reliable studies and data in this group to support a standard therapy. Currently, both maternal and fetal factors, such as cancer clinical stage, lesion size and gestational age determine management.

In early stage cervical cancer, lymph node metastases are found in up to 20% of patients, which is considered the most important negative prognostic factor. To date, all non-invasive diagnostic procedures do not precisely reflect nodal status. Histopathologic evaluation of the lymph nodes mainly before 20 weeks of gestation, is a crucial parameter to select the most appropriate treatment strategy. Maintenance of pregnancy appears to be safe in a lymph node negative patient, whereas delay of oncologic therapy for fetal benefit in a patient with a nodal metastasis should not be recommended.

We performed laparoscopic lymphadenectomy in 13 patients in the first half of pregnancy and report no complication to the mother or to the fetus related to the surgery. The knowledge of the tumor biology gives a sound basis for the management of mother and fetus which can vary between expectative observation till term, neoadjuvant chemotherapy, or immediate treatment with termination of pregnancy.
Implantation of the fertilized egg into the uterine decidua establish a contact with maternal circulation which is crucial for the success of pregnancy. Prothrombotic state such as thrombophilias may interfere with these processes with thrombosis, abnormal implantation and trophoblast invasion and other as yet unknown mechanisms, which may lead to placental vascular complications (PVC). There is increasing evidence regarding the specific association of PVC such as severe preeclampsia, fetal loss, fetal growth restriction (FGR), abruptio placentae and thrombophilias. The overall prevalence of PVC is approximately 8%, however these complications accounts for 75% of fetal morbidity and mortality regardless of thrombophilias. It is also evident that prior history of any of these pregnancy complications is a strong predictor of their occurrence in a subsequent pregnancy and prior poor pregnancy outcome is associated with a significantly higher risk of subsequent pregnancy outcomes. When PVC are associated with thrombophilia the recurrent rate in subsequent pregnancies may be as high as 54%. Several recent systematic reviews and metaanalysis clearly demonstrate association between severe preeclampsia, FGR, abruptio placentae and early and late fetal loss. Early fetal loss is associated with the factor V Leiden (FV) the prothrombin mutation (PTM), hyperhomocysteinemia and APS while late fetal loss is associated also with protein S. Preeclampsia is associated with FV, PTM, hyperhomocysteinemia and APS. Placental abruption is associated with FV and PTM and FGR is associated with PTM and APS.

Because of the high recurrence rate of PVC and the risk for thromboembolism in these women, women with PVC and thrombophilias are candidates for anti-thrombotic therapy in subsequent pregnancies. Increasing number of reports indicate that intervention in subsequent pregnancies with anti-thrombotic therapy such as low molecular weight heparin (LMWH) may dramatically improve outcome in these women and prevent recurrence of PVC.
Recurrent pregnancy losses and thrombophilia – possible therapeutic approaches

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Recurrent loss of two or more consecutive pregnancies occurs in about 5% of the pregnant women. Pregnancy loss is a multifactorial disease including genetic, acquired and environmental determinants, and is associated with thrombophilic diseases/imbalances. But the variable association between constitutional thrombophilias and pregnancy loss cannot be currently viewed as a causal one. Several studies have suggested that low molecular weight heparine (LMWH) may be beneficial with regard to adverse pregnancy outcome in patients with thrombophilia and a past history of adverse pregnancy outcome. However, as yet there are no adequately powered, randomised, controlled trials with an untreated or placebo arm in order to confirm the suggestion of benefit. Such, much needed, trials are currently underway and their results will be important in informing evidence-based practice in this area.

The observation of the German ETHIG study in 810 pregnant women with thromboembolic risks that pregnancy loss are reduced from 35% to 11% using LMWH prophylaxis, encouraged us to initiate such a prospective randomized trial comparing Dalteparin prophylaxis (5000 IE) with placebo for preventing further miscarriage in women with previous recurrent pregnancy loss (ETHIG II). The study design and first results of the ongoing study are presented. Although low molecular weight heparin is safe in pregnancy it is not completely without risks, and until clear benefits from such intervention are available such treatment must be considered experimental while we await the results of the ongoing randomised controlled trials.
Thrombophilia and preeclampsia/HELLP-syndrome

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Preeclampsia (PE) is still a leading cause of maternal and neonatal morbidity and mortality. In a two-hit model of PE, in which a triggering event is exacerbated by other factors, thrombophilia are the exacerbating factor, or second hit. More than 70 studies have investigated the association between inherited and acquired thrombophilias and PE, yielding contradictory results. The total prevalence of thrombophilias in women with PE has found to be 65% compared to 18% in controls. In the largest systematic review the risk of PE was significantly associated with heterozygous factor V Leiden and heterozygous prothrombin mutation, MTHFR homozygosity, the presence of anticardiolipin antibodies and hyperhomocysteinemia. Other systematic reviews/metaanalyses are controversial with evidence supporting or refuting this association. The prevalence of thrombophilias and PE is strongly influenced by various confounders as ethnicity, severity of illness and methods of testing. Mild PE is not associated with thrombophilias, whereas the risk of severe early-onset PE is significantly related to inherited and acquired thrombophilias. In women with severe PE and thrombophilia the rate of maternal complications, IUGR, early delivery < 32 weeks’ gestation and low birthweight infants is significantly higher as compared to PE and no thrombophilia. Thrombophilia is also associated with a 2.5 fold increase in the recurrence risks of PE. Data describing the relationship between fetal thrombophilia and PE are limited. While the recent ACCH guidelines recommend screening only for antiphospholipid-antibodies, other guidelines favour complete thrombophilia screening in patients with severe PE/HELLP syndrome < 34 weeks’ gestation. For women considered high risk for PE, low-dose aspirin is recommended, women with a previous severe PE/HELLP syndrome and a genetic thrombophilia (heterozygous FVL and prothrombin mutation) should be offered low-dose heparin and aspirin in subsequent pregnancy, however, prospective randomized studies are urgently needed.
Secondary data analyzes in perinatology

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In contrast to other special areas in epidemiology perinatal epidemiology has to deal with three individuals, the mother, father and the child. Thus different - although dependent – risk profiles interact and influence the outcomes of both, mother and child. To study these most complex risk factor patterns and associated outcomes, birth cohorts are defined and followed-up over years, some starting data collection already before pregnancy (e.g. National Children’s Study). However, such prospective data collection procedures are time-consuming, expensive and prone to selection bias due to loss-to-follow-up. An alternative/additional approach is the analysis of secondary databases, i.e. analyzes of data collected for a different purpose than the research question. Data sources, such as hospital data, claims data, linked birth and death certificates or data from quality assurance programs can be used for research. But the beauty of time and cost saving is often only skin-deep: Study design, in- and exclusion criteria, in- and external validation procedures, analytical methods and model validation procedures are challenging and often misleading. In addition, guidelines for good secondary data analyzes are not fully established yet. Examples for risks and benefits of secondary data analyzes are presented.
BMI and weight gain in pregnancy: Epidemiology and impact

Karl Bergmann

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During recent decades, the prevalence of BMI values indicating overweight and obesity increased significantly in women of reproductive age. Also, there is a trend for greater weight gain during pregnancy: in a study representative for Germany (KiGGS), average pregnancy weight gain increased from 13kg in 1986 to 15kg in 2005, a difference of as much as 2kg in only 20 years. During the same period, the proportion of newborn infants exceeding a birth weight of 4,000g increased from about 9 to 12%. Pre-existing obesity as well as excessive weight gain in pregnancy are known risk factors for diabetes, hypertension, congenital anomalies, premature, and still birth, neonatal macrosomia, and complications during delivery. High weight gain during pregnancy fosters the development of obesity, metabolic syndrome and type II diabetes of the women in their later life. Macrosomic newborns tend to develop high BMI values in their adult ages. It is speculated that more macrosomic newborns of overweight pregnant mothers or as a consequence of excessive weight gain in pregnancy may contribute to the increase in the prevalence of overweight and obesity in our populations constituting a "snowball effect". However it seems that this effect may be grossly overestimated by using the BMI as an indicator. Macrosomic newborns not exposed to pathologic metabolic conditions in utero may even have developmental and health advantages. Considerations on different types of high fetal growth rates will be included.
Ambiguous definitions in perinatology

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Definition of the perinatal period is not as clear-cut as it looks at first glance. Standards for estimation of gestational age at birth vary. The International Classification of Diseases (ICD-10) presupposes the last menstrual period as the starting point, with “best clinical estimate” as alternative if this date is not available or uncertain. Ultrasound has increasingly replaced menstrual dates in countries where ultrasound is an integral part of prenatal care. Ultrasound standards vary in different populations and are typically based on “supernormal” pregnancies with unquestionably certain dates, spontaneous term labors and an in-built addition of two to three days to the 280-day rule, as the expected term date. Ultrasound dating therefore automatically changes the distribution of gestational age to a narrower term range compared to last menstrual period dating, besides a parallel shifting of the whole population to younger gestational age at birth, Resulting in a higher proportion of pre-term and fewer post term births. This change of standards has led to changes of official registration in medical birth registries, which have largely gone unheeded by those who use the data for comparative and research purposes.

In some countries civil notification of stillbirth starts at 28 completed gestational weeks, precluding the enumeration of stillbirths between 22 and 28 weeks. To avoid enigmatic definitions of gestational length, age is in some instances replaced by birth-weight of 1,000 grams or more. Similarly, 500 grams may replace 22 weeks. Because these limits for weight and age do not fully correspond, another ambiguity is introduced.

In perinatal research, definitions should always be minutely explained to avoid confusion. In clinical practice, antenatal care providers must be aware of the changing concept of gestational age, particularly for post term advice and intervention.
Evidenced-based versus reality-based methods in assessing perinatal outcomes

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Objective: To introduce a “new” level of evidence in Obstetrics (Reality-based medicine)

Background: In Obstetrics, the numerous shortcomings in evaluating “evidence” objectively has led to situations where there may be disagreement between the conclusions drawn from the “highest” level of evidence studies (RCTs) and those of real-life observational studies.

Methods: Perinatal outcome associated with the use of the two most commonly used obstetrical tests (EFM and ultrasound) was assessed as determined by published RCT’s and real-life observational studies.

Results: Reality-based observations in the US revealed that the natural consequences triggered by the use of EFM and/or ultrasound are increased obstetrical intervention rates, labor inductions, caesarean deliveries and, consequently, indicated preterm births. The steady increase in obstetrical interventions (caesarean deliveries and labor inductions) and consequently indicated preterm births, has led to decreasing perinatal mortality rates primarily due to less stillbirths and less early neonatal deaths. More importantly, among all clinical subtypes of preterm births, the steepest decline in perinatal mortality occurred among the indicated preterm births. Careful analysis of trends in fetal deaths in US, after the introduction of fetal surveillance in the mid-1970’s, shows a dramatic decline in fetal death rates at >28 weeks, whereas the fetal death rate has remained unchanged for the very early gestations (20-27 weeks) where fetal surveillance had been rarely used.

Conclusion: Reality-based observations strongly suggest that fetal surveillance with its accompanying obstetrical interventions are etiologically linked to the decreasing fetal death rate. This conclusion is in conflict with most RCTs which have failed to show any benefit. It is time to introduce a new level of evidence, “reality-based”.

Challenges of pain management in ventilated preterm infants

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Background: The large majority of infants admitted to a neonatal care unit (NICU) will require some form of respiratory support for a varying duration. As part of their intensive care these infants undergo a high number of painful procedures. Pain management, including assessment of pain and its treatment is highly challenging in these patients. Pain reaction is usually damped by sedatives and consequently pain assessment is affected and questionable in its reliability. Despite well-conducted studies in ventilated preterm neonates, the best way to provide analgesia is not known. Increasingly, non-pharmacological pain relieving interventions are discussed to provide pain relief. This type of intervention includes methods that involve reducing the sensitivity of the neonates during and after painful procedures, which have been shown to effectively reduce pain from minor procedures in neonates.

Methods: A randomized placebo controlled trial in two NICUs in Switzerland with a sample of 30 mechanically ventilated preterm infants was conducted to test the hypothesis that an intermittent dose of morphine reduces pain during endotracheal suctioning and that subsequent “multisensorial stimulation”, as a non-pharmacological comforting intervention, helps infants to recover from experienced pain.

Results: Morphine did not lead to any pain relief from ETS as measured by three pain scales. Nor did the comforting intervention of “multisensorial stimulation” show any effect. The psychometric properties of the used instruments are questionable in this patient population.

Conclusion: The use of morphine for pain relief during ETS and the use of multisensorial stimulation as a comforting method for very low birth weight children should be critically discussed. Future research should focus on options among other non-pharmacological interventions for pain relief and for the psychometric testing of existing pain assessment tool related to ventilated infants.
Persistent pulmonary hypertension of the newborn (PPHN) is common in neonates with respiratory failure. It is characterized by pulmonary hypertension and extrapulmonary right-to-left shunting across the foramen ovale and ductus arteriosus. Inhaled nitric oxide (iNO) is a potent and selective pulmonary vasodilator. In many clinical situations, iNO will improve oxygenation by improving ventilation-perfusion matching in the failing lung. Since the FDA approval of inhaled nitric oxide for the treatment of hypoxic respiratory failure (HRF) in the term newborn in the late 1990’s, it has been suggested that iNO might also benefit the sick infant, and, in particular, reduce the incidence and severity of bronchopulmonary dysplasia (BPD)/chronic lung disease (CLD). These problems affect premature infants, significantly contributing to their morbidity and mortality. Several clinical trials have tested the use of iNO in preterm infants, with widely differing inclusion criteria, treatment regimens and outcome measures. The Results have been broadly mixed. Inhaled nitric oxide could potentially be used for the prevention of BPD, for treatment of BPD, or as rescue therapy in these preterm infants. Lately, there are some publications describing “remote” effects of iNO, including angiogenesis and maturation on the developing brain in animal models. This presentation will review the pathophysiology and treatment of PPHN, the use of iNO in trials in term infants, and, finally, the Results of recent iNO trials in preterm infants.
Volume targeted ventilation in the newborn: A variation on the theme?

Win Tin

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Despite the introduction of newer strategies such as high-frequency ventilation, inhaled nitric oxide, extracorporeal membrane oxygenation and partial liquid ventilation, conventional mechanical ventilation remains the primary treatment for respiratory failure in newborns. This has usually been accomplished with traditional time-cycled, pressure-limited ventilation (TCPL), designed to deliver a volume of gas with a pre-set peak inspiratory pressure (PIP) during a defined cycle time. As a Result, the peak pressure at the proximal airway remains constant but the tidal volume delivered to the lungs is variable depending on the underlying pulmonary and chest wall mechanics. Thus, when the lungs are stiff, tidal volume delivery is lower at the same peak pressure than when the lungs are more compliant. This inconsistency in tidal volume delivery may be undesirable particularly in very preterm infants because both over expansion (volutrauma) and under expansion/collapse (atelectotrauma) are thought to contribute to pulmonary injury sequence. This has led to the introduction of newer forms of ventilation, which aim to deliver a desired tidal volume irrespective of the underlying lung mechanics.

Volume targeted modes of ventilation can be provided in two ways: Volume Controlled Ventilation (VCV), where primary target is the delivery of a set tidal volume irrespective of lung compliance; or hybrid modes, which are essentially pressure-targeted but aim to deliver the tidal volume within a set range using computer controlled feedback mechanism.

Compared to TCPL, Volume targeted modes of ventilation are relatively new to the neonatal intensive care, and there are only a few published controlled trials testing these modes in the newborn population with high risk of lung injury. Nevertheless the evidence available so far is encouraging.

Suggested Reading:
The use of progesterone and 17-alpha hydroxyprogesterone caproate in the prevention of preterm delivery

Fabio Facchinetti

Modena, Italy

Preterm Delivery (PTD) is defined by the World Health Organization (WHO) as birth before 37 completed weeks of gestation. In western countries, PTD accounts for over 75% of all perinatal morbidity and mortality. The social importance of PTD derives from the consideration that it causes near three quarter of neonatal deaths not caused by malformations.

Progesterone is a steroid hormone which plays a crucial role in each step of human pregnancy. Early in pregnancy progesterone is produced by the corpus luteum and it is fundamental for pregnancy maintenance until placenta takes over this function at 7-9 weeks of gestation. Late in pregnancy, the role of progesterone is less clear: certainly, it may be of importance in maintaining uterine quiescence in the latter half of gestation by limiting the production of stimulatory prostaglandins and inhibiting the expression of contraction-associated protein genes (ion channels, oxytocin and prostaglandin receptors, and gap junctions) within the myometrium.

We performed a Review including those controlled clinical studies (RCTs) that have used either 17 Hydroxy Progesterone caproate (17P), or Progesterone (P) in order to avoid or reduce the incidence of preterm delivery, in populations of women at increased risk of preterm birth.

We conclude that: 1) the treatment with 17P reduces the incidence of PTD in pluriparous women with a previous history of PTD or recurrent abortions (3 RCTs); 2) 17P also reduces PTD in nulliparous women with an actual risk (either contractions or cervical shortening) (1 RCT); 3) the treatment with P also reduces PTD in nulliparous women, namely in the presence of a silent cervical shortening (2 RCTs); 4) 17P has no efficacy in multiple pregnancy (2 RCTs) and it is proven not to have adverse effects on the infants (1 RCT).
Towards an intra-uterine neurologic examination

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In modern perinatology, there is growing interest in the assessment of the integrity and activity of the fetal central nervous system (fCNS). As it is not yet possible to test the fCNS directly, we can only use indirect methods. First, we focused on the non-invasive observation of fetal behavior. Fetal behavior was studied by investigating the association between fetal heart rate patterns and ultrasonic observations of body and eye movements. The maturation of fetal motility and changes of motility patterns have led to the definition of four fetal behavioral states, already in 1982, but the definitions are still valid. Valid reference ranges appropriate for the gestational age have been published later.

The obvious next step, was to see whether we could evoke intra-uterine reflexes, thus no longer non-invasive. We were able to evoke an intercostal-to-phrenic-inhibitory reflex (IPIR): compression of the ribcage Results in an apnoea. This seemed an interesting approach, but they were not able to find a different Result in a group of growth-retarded fetuses.

Fetal habituation, i.e. the cessation of response to a repeated stimulus, is another test. We showed that fetuses fail to respond after a number of vibro-acoustic stimuli. When the test was repeated after 10 minutes and after 24 hours, this number of stimuli was significantly lower. This was the first indication that the fetus already has a memory. In 2009 we have shown that fetal learning exists: from 34 weeks on onward is capable of remembering a stimulus after four weeks.

Prenatal neurology – Fact or fiction

Franz Kainer

Munich, Germany

The possibility to assess the functional condition of the fetal nervous system is of great importance to the obstetrician, since a considerable part of early brain damage is of prenatal origin. However, Levine concluded in his paper “Fetal neurology- fact or fiction” in 1993 that prenatal neurological assessment is not feasible. Prechtl stated in 1997 that the qualitative assessment of General movements is an excellent marker of brain dysfunction in neonates. The fact that the same criteria can be used for the fetus this method is also attractive for the prenatal neurological examination. In the meantime new methods (MRI, four-dimensional ultrasound) for the examination of the fetal brain are available. Kurjak published the application of three-dimensional (3D) and four-dimensional ultrasound (4D) in studies about fetal behavior. These techniques enable simultaneous spatial imaging of the entire fetus and its movements. Despite these new techniques there is still a lack of prospective studies demonstrating the clinical usefulness of these methods. In the meantime we have to conclude that fetal neurology is more fiction than fact.
Recent advances in fetal neurophysiology

Aida Salihagic Kadic, Maja Predojević, Milan Stanojević, Asim Kurjak

Zagreb, Croatia

The prenatal period of life has considerable influence in shaping future development and behavior. Functional development of the fetal brain begins as early as the late embryonic period. During the nine months of gestation, a repertoire of fetal activities constantly expands, correlating precisely with the structural development of the central nervous system (CNS). In our longitudinal study fetal movements have been followed through all trimesters by four-dimensional (4D) sonography. Results have shown increasing frequency of the fetal movements during the first trimester. A tendency towards decreased frequency of facial expressions and movement patterns with increasing gestational age from second to third trimesters has been noticed. Extensive studies into the movement patterns have been conducted, tracing all newborn movement patterns back to the prenatal period. We confirmed the existence of prenatal-neonatal continuity even in subtle, fine movements such as facial mimics. Knowing that fetal behavioral patterns fairly correlate with the development of the CNS and that quality of fetal movements reveals the integrity of the CNS, in our recent research we compared the fetal behavior in normal and in high risk pregnancies, and proposed a new scoring system for fetal neurobehavior based on prenatal assessment by 3D/4D (three-dimensional/four-dimensional) sonography. This preliminary work may help in detecting fetal brain and neurodevelopmental alterations due to in utero brain impairment. The advanced imaging techniques such as 3D/4D sonography, indeed have revealed invaluable details of fetal behavior and its development, opening the door to a better understanding of the prenatal functional development of the CNS.
Neurobehavioral fetal to neonatal continuity

Milan Stanojevic, Asim Kurjak, Brivoj Miskovic

Zagreb, Croatia

Aim: to compare the quantity of behavioral patterns and facial expressions pre- and postnatally in low risk pregnancies. To compare Kurjak's Antenatal Neurological Assessment (KANET) of fetuses from high risk pregnancies with Amiel Tison Neurological Assessment at Term (ATNAT) and General Movement (GM) assessment at premature age.

Methods: 28 out of 45 pregnant women in the 3rd trimester of normal pregnancy and 28 term newborns were included in the study. 117 out of 125 fetuses were assessed in the 2nd and 3rd trimesters of high risk pregnancy of which 9 had borderline and 3 abnormal KANET test. All fetuses were assessed by 4D ultrasound. Newborns underwent postnatal ATNAT and GM assessment.

Results: Hand to mouth and hand to face movements were more frequent in fetuses than in neonates, while other hand movements were less frequent in neonates. Facial expressions were the same pre- and postnatally. Spearman rank order correlation test reached statistical significance between the fetuses and the newborns in hand movements. In 12 fetuses from high risk pregnancies with borderline or abnormal KANET postnatal ATNAT was normal in 10, borderline in 1 and abnormal in 1. GM assessment at premature age revealed 1 definitely abnormal, 1 abnormal and 10 normal suboptimal findings.

Conclusion: There is continuity between fetal and neonatal movement patterns concerning the quantity of hand movements and facial expressions in low risk fetuses. In high risk fetuses with borderline or abnormal KANET, postnatal ATNAT and GMs may be normal, borderline or abnormal. There is a need for further investigation of this intriguing finding.
Invited Speaker
Parallel session 15: Fetal and neonatal neurodevelopment

Fetal neurodevelopment

Zahra Nese Kavak

Istanbul, Turkey

The development of the human central nervous system (CNS) begins in the early embryonic period. Fetal neurodevelopment is imperatively important as cerebral palsy is the most common disability in childhood. Recent researches suggests that 70-80% of CP cases are due to prenatal factors. Prenatal imaging technologies such as transvaginal ultrasound, three-dimensional ultrasound, magnetic resonance imaging have remarkably contributed prenatal fetal central nervous system evaluation. Fetal neuroimaging “neurosonography” by the help of 3D/4D imaging is easy, non-invasive, and reproducible methods. Different modes like tomography, surface rendering, multiplanar section evaluation of 3D and 4D US made it possible to objectively evaluate the data, to store and reevaluate or share the data with other colleagues like neurosurgeons and neurologists. Fast MR imaging gives excellent view of fetal CNS structures and is very popular as FMR imaging doesn’t give ionizing radiation and it supplies excellent soft tissue contrast together with multiple reconstruction planes. Recent researches show that neuroimaging by ultrasound and MR imaging is the most reliable modality for disclosure of silent encephalopathy. There are numerous environmental factors studied on fetal neurodevelopment. For example, prenatal stress exposure, maternal smoking, alcohol, toxins/drugs, nutrition, psychosocial stress and infection during pregnancy can create changes in neurodevelopment and in the set point of neuroendocrine systems. Some drugs or vitamin deficiencies are also studied nowadays about the fetal neurodevelopment. Some of them are prenatal lead exposure, calcium supplementation and iron deficiency.

There is also evidence about especially extremely preterm infants are at high risk for poor growth and impaired neurodevelopment. Fetal growth is very important with long-term motor development and cognitive function. Early diagnosis of fetal growth restriction can therefore reduce the severity of neurological sequelae.

Using 4D US it is possible to evaluate normal neurological development. Prenatal movements are an expression of development of fetal CNS,. Assessment of fetal behavioral patterns could give us insight into the integrity of fetal central nervous system and enable the early detection of cerebral dysfunctions. Therefore combination of fetal neurological assessment together with fetal behavior and fetal neuroimaging can help us in understanding of complex neurodevelopmental events.
The assessment of fetal neurobehavior in diabetic patients by 3d-4d sonography

Ahmed Badreideen

Doha, Qatar

It is known that fetuses of women of type-I diabetes are at increased risk for malformation, macrosomia and impaired development of the central nervous system. Fetal hyperinsulinism can develop even in mothers with seemingly sufficient metabolic control during pregnancy. This is an important additional factor that influences the neurological development of the fetus.

In prospectively planned research at several international centers we applied our recent prenatal neurological test (KANET – J Perinat Med 2007) to answer following questions:

1. Does maternal type-I diabetes influence the fetal nervous system?
2. Is such an influence expressed in abnormal scoring?
3. What is the relationship between pre- and postnatal scoring Results?
4. What is the relationship between fetal neurobehavioral assessment and various parameters of maternal diabetes?

We will report about 100 diabetic pregnant patients examined by 3D-4D sonography and in particular about two cases of antenatal detected cerebral palsies in diabetic patients.
Ethical challenges for innovation and research in perinatal medicine

Frank A. Chervenak

New York, USA

The future of perinatal medicine depends on responsible innovation and research. Innovation occurs when a new diagnostic or therapeutic intervention is introduced into the clinical setting for the first time. When innovation appears promising and physicians want to repeat the intervention, such investigation becomes research because physicians are seeking generalizable knowledge that can be applied in the future clinical care. The ethics of innovation and research in medicine require that innovation and research in perinatal should be conducted to the highest scientific and ethical standards. The ethical standards should be based on the ethical concept of the fetus as a patient. Based on this central ethical concept of perinatal medicine, this presentation will identify ethical criteria for innovation, for clinical research, and for the transition from research to standard of care. The goal will be to provide investigators in perinatal medicine with ethically justified and clinically useful criteria that can then be used to design, conduct, and evaluate responsible innovation and research in perinatal medicine.
Human reproductive cloning in 21 century?

Joseph G. Schenker

Jerusalem, Israel

Reproductive cloning is used to describe the process of asexual reproduction. The cloning technology involves taking the nucleus from a somatic cell and then inserting that nucleus into an unfertilized egg that has had its own nucleus removed. The newly reconstructed embryo thus contains the entire genetic makeup of the donor somatic cell (except for mitochondria DNAs) and when transferred into the uterus of a surrogate mother can develop into an individual genetically identical to the nuclear donor. by transplanting nuclei from embryonal or somatic cells into enucleated cells. Cloning via nuclear transfer has succeeded in numerous mammalian species involving the use of various somatic cells as donors. Successes in animal cloning have been accompanied by many failures: a few percent of nuclear transfer embryos survive to birth and, of those, many die soon after from serious developmental problems. Scientist opposes cloning humans, primarily because of the high failure rate and because the technology for detecting genetic abnormalities used in routine prenatal diagnosis cannot detect problems in epigenetic programming. Faulty epigenetic reprogramming can cause abnormal expression of any gene, which is consistent with the wide spectrum of developmental and physiological defects seen in cloned animals. Reproductive cloning has created various ethical concerns and regulation debate. The United Nations and most governments around the globe have called for a ban on reproductive cloning in humans. The medical, social, legal, political and religious aspects will be discussed.
Prevention of mother to child transmission of HIV in Eastern Africa

Gundel Harms-Zwingenberger

Berlin, Germany

Every year, 700,000 children are infected with HIV worldwide, most of them through vertical transmission in sub-Saharan Africa. The risk of transmission in developing countries during pregnancy, labor and via breast feeding lays at about 30% and is highest perinatally. Since 2001, the German Government through the German Technical Cooperation supported a program for PMTCT of HIV in Kenya, Tanzania and Uganda, coordinated by the Institute of Tropical Medicine, Charité-Universitätsmedizin Berlin.

Comprehensive PMTCT Programmes including ART programs were integrated into about 200 health facilities and more than 220,000 women made use of the offer. While in the first phase nevirapine single dose, which is still the most commonly applied regimen for PMTCT in resource-limited areas was used as prophylaxis, currently the WHO-recommended extended antiretroviral regimen is applied.

Operational research activities comprised KAPB studies on mother-to-child transmission in different population groups, on practice of infant nutrition, minimal requirements for program implementation, different strategies of nevirapine (NVP) administration, different methods to simplify treatment monitoring, cost-benefit analyzes and, studies to increase male participation.

In mother-child pairs, concentrations of nevirapine over time were assessed in different body compartments such as plasma, breast milk, cervicovaginal- and oropharyngeal secretions, and time-concentration profiles developed. Prolonged low-level concentrations of nevirapine may foster resistance formation. To assess the extent of NNRTI-associated resistance mutations of the HIV-genome, a highly sensitive allele-specific real time PCR was modified for the HIV subtype A and D. The NVP-resistant HIV minorities detected in plasma and breast milk of Ugandan women emerged later than 2 weeks after the administration of the prophylaxis and persisted for prolonged periods. The implications for long-term antiretroviral treatment are not yet clear. Drug resistance formation in the context of the WHO-recommended extended antiretroviral regimen is currently investigated in mothers and children in Tanzania.
Mode of delivery and mother-to-child transmission of HIV: Unanswered questions

Jennifer S. Read

Bethesda, USA

Ten years ago, two landmark studies demonstrated the efficacy and effectiveness of caesarean delivery before labor and before rupture of membranes (SCS) for preventing mother-to-child transmission (MTCT) of HIV. Results from the randomized clinical trial conducted in Europe demonstrated an 80% reduction in the rate of MTCT of HIV among women randomized to SCS. The individual patient data meta-analysis of over 8,000 mother-infant pairs from North America and Europe demonstrated a 50% lower transmission rate among those with SCS, and lower transmission with SCS was observed both among mother-infants pairs with and without antiretroviral prophylaxis. Subsequent studies evaluated the safety and cost effectiveness of SCS for preventing transmission. In Europe and other resource-rich settings, the benefits of SCS for HIV-infected women with plasma HIV RNA concentrations (viral loads) over 1,000 copies/mL generally outweigh the increased risk of minor postpartum morbidity. SCS for preventing MTCT of HIV has been shown to be cost effective in several studies. Infant respiratory morbidity among HIV-exposed infants according to mode of delivery is now being evaluated. The most important unanswered question regarding use of SCS as an intervention to prevent MTCT of HIV is whether SCS has a role in the management of women with low viral loads and/or who are using combination antiretroviral drug regimens, including highly active antiretroviral therapy. Additionally, the appropriate role of SCS among HIV-infected women in resource-limited settings, where medical infrastructure and staffing may be limited and where HIV prevalence rates may be very high, remains to be defined.
Management of HIV infection in pregnancy and the newborn

Richard Thwaites

Portsmouth, UK

The world HIV pandemic began in 1981. Whilst long term ‘control’ of the virus is now possible, prevention of horizontal infection and cure remain elusive. Prevention of vertical transmission is now the norm, at least in the developed world1.

Key measures for success in UK:
- Free access to antenatal/sexual health clinics
- Near universal pregnancy HIV screening
- Multiprofessional team approach.

Our clinic serves an urban/rural population of 550,000. Patients have benefited from comprehensive guidelines2. Efforts are made to achieve UDVL, allowing selected women to opt for normal delivery. Resistance testing, ‘adherence’ and close monitoring are essential. Breastfeeding is discouraged. Infants are monitored for >18 months to determine infection status. Low risk infants receive AZT 4mg/kg BD for 4 weeks and are tested for HIV DNA/RNA at birth, 6 and 12 weeks. Uninfected infants are then referred for BCG. HIV antibody testing is recommended at 18 months.

High risk infants present special challenges. Locally these comprised 2 groups since 2001:
1. Preterm: Two <28 weeks. Five born at 28-36 weeks were all from multiple pregnancies.
2. Mothers who declined any treatment and had high viral loads at delivery: Two families generated a disproportionate workload requiring close additional involvement of social care. One baby was discharged home after birth, with daily midwifery supervision for 4 weeks and the other was fostered.

These 9 infants received HAART (IV/oral AZT, Lamivudine for 4 weeks, Nevirapine for 2 weeks, doses depending on age/gestation). All had negative for HIV PCRs at >3 months.

We screen older children of newly diagnosed women. Locally, most infected children were identified this way; none were born in the UK.

Conclusion: Where resources allow and patients access them, vertical transmission should be avoidable in nearly all cases. Management of HIV+ve children and pregnant women still present significant challenges.

References
Universal antiretroviral therapy for pregnant and breastfeeding HIV-infected women: Towards the elimination of mother-to-child transmission of HIV-1 in resource-limited settings?

Renaud Becquet

Bordeaux, France

Prevention of mother-to-child transmission of HIV-1 (MTCT) remains a challenge in most resource-limited settings, particularly in Africa. Single-dose and short-course antiretroviral (ARV) regimens are only partially effective and have failed to achieve wide coverage despite their apparent simplicity. More potent ARV combinations are restricted to pregnant women who need treatment for themselves but are also infrequently used. Furthermore, postnatal transmission via breastfeeding is a serious additional threat. Modifications of infant feeding practices aim to reduce breast-milk HIV transmission: replacement feeding is neither affordable nor safe for the majority of African women, and early breastfeeding cessation (e.g. prior to 6 months of life) requires substantial care and nutritional counseling to be practiced safely. The recent roll out of ARV treatment has changed the paradigm of prevention of MTCT. To date, postnatal ARV interventions that have been evaluated target either maternal ARV treatment to selected breastfeeding women, with good efficacy, or single-drug post-exposure prophylaxis for short periods of time to their neonates, with a partial efficacy and at the expense of acquisition of drug-related viral resistance. We hypothesize that a viable solution to eliminate pediatric AIDS lies in the universal provision of fully suppressive ARV regimens to all HIV-infected women through pregnancy, delivery, and covering the entire breastfeeding period. Based on the available evidence, we suggest translating into practice the recently available evidence on this matter without any further due.
The ethical dilemma of withholding or withdrawal of neonatal intensive care

Victor Yu

Clayton, Australia

Among the many neonatal ethical dilemmas, the one which neonatologists are faced with on a regular basis involves the issue of selective non-treatment, that is, clinical decisions made after the birth of a live-born infant to either withhold or withdraw neonatal intensive care in certain clinical scenarios. If doctors believe that the infant has little prospect for intact survival, their management would be suboptimal and that would create the self-fulfilling prophecy of an adverse outcome. Therefore, a policy establishing criteria for withholding life-sustaining treatment must be developed with proper consideration of the prevalent cultural, social, religious and economic factors, which are vastly different between developed and developing countries. After the initiation of neonatal intensive care, there are infants whose subsequent clinical course will indicate that further curative efforts are futile or lack compensating benefit. Therefore, a policy establishing criteria for withdrawing life-sustaining treatment must also be developed, to allow the appropriate use of palliative care in these instances. The clinical situations in which selective non-treatment is taking place in the neonatal intensive care unit are: (1) when death is considered to be inevitable whatever treatment is provided, (2) even when death is not inevitable, there is a significantly high risk of severe physical and mental disability should the infant survive, and (3) when survival with moderate disability is possible, but the infant is likely to experience ongoing pain and suffering, repeated hospitalization and invasive treatment, and early death in childhood. The principles underlining selective non-treatment should be the same for developed and developing countries, although the criteria appropriate in such diverse settings would differ. The proper management of the ethical dilemma of withholding and withdrawal of neonatal intensive care must involve less medical paternalism and more informed parental involvement, especially in developing countries.
Clinical trials of neuroprotection following birth asphyxia

Denis Azzopardi

Despite extensive experimental studies of neuroprotection following asphyxia, relatively few clinical studies have been carried out. Initial studies used pharmacological intervention to reduce free radical or excitotoxic mediated brain injury, but were mostly unsuccessful partly because of logistical problems in enrolling sufficient numbers of subjects very soon after birth or because of adverse effects. Recently Results from randomized trials of hypothermia started with 6 hours and maintained for 72 hours confirm that cooling to 33.5°C reduces mortality and improves neurological outcomes in survivors. However several questions concerning therapeutic hypothermia such as whether cooling is effective beyond 6 hours after birth or whether it is modified by the severity of encephalopathy cannot be addressed with the current data, but further studies addressing these issues are on going. Despite these concerns, hypothermia is now rapidly becoming the standard of care in developed countries but its safety and feasibility in resource poor countries has not yet been confirmed. Following these studies focus has moved towards reducing the progressive phase of brain injury that occurs over several days following asphyxia and is thought to be primarily involving apoptosis. Clinical trials targeting these mechanisms such as with erythropoietin and xenon gas are underway and preliminary Results are very promising. Therefore there is now conclusive evidence from clinical trials that intervention following perinatal asphyxia is feasible and effective. The emphasis in future studies will be to determine modifying clinical factors, identifying synergistic therapeutic interventions and exploring these therapies in other patient groups, including preterm infants.
Inhibition of mitochondrial outer membrane permeabilization: Effective strategy for brain protection?

Henrik Hagberg

London, UK

The etiology of brain injury in term and preterm infants is multi-factorial but cerebral hypoxia-ischaemia (HI) and infection-inflammation are likely contributors. There is evidence that brain injury after severe birth asphyxia develops with a delay, and recent hypothermia studies support that post-HI neuroprotective treatment is a clinical possibility. There are several candidate interventions like erythropoietin, xenon, melatonin and topiramate that are currently being investigated in clinical and preclinical studies for possible use as the next generation of neuroprotective therapy. Our hypothesis is that mitochondrial permeabilization (MP) is a key event in the pathophysiology of secondary brain injury shifting a reversible condition into irreversible cell death. HI triggers a number injurious events: release of excitatory amino acids, increased intracellular calcium, accumulation of nitric oxide and other reactive oxygen species leading to DNA damage and induction of p53, inflammasome/NFkB and death receptor activation, and loss of trophic factor support. At a certain threshold level these upstream “stressors” will increase the pro- vs. anti-apoptotic Bcl-2 family protein balance leading to MP, leading to release of pro-apoptotic proteins and caspase- and non-caspase dependent DNA fragmentation and brain injury. In contrast to adult brain ischemia, MP in neonatal CNS injury is unrelated to the mitochondrial transition pore but is caused by a a conformational change and translocation of Bax to mitochondria with formation of a Bax/Bak pore that can be pharmacologically manipulated. For example administration of a caspase-2 selective inhibitor or a novel Bax-inhibiting peptide effectively block MP and brain injury and constitute potential targets for future neuroprotective treatment in combination with hypothermia.
Invited Speaker  
Panel discussion 5: Brain protection  

Perinatal asphyxia: New strategies for neuroprotection  

Jose Martinez-Orgado  
Madrid, Spain

In addition to hypothermia, different strategies are currently being investigated in order to reduce postasphyctic newborn brain damage. Among those more feasible to be used in human, erythropoietin is the one with best Results in experimental models, acting on several mechanisms leading to hypoxic-ischemic cell death and showing neuroregenerative effects; however, concerns about its possible effects on retinal development have to be elucidated before using it in humans. Topiramate, as an AMPA receptor antagonist, offers promise Results, in particular in association with hypothermia, but there is little experience on its use by IV route and in newborns. Stem cell therapy offers also good experimental Results, but its therapeutical window is not known. Cannabinoids emerge as a promise tool for preventing and/or reducing brain damage after HI. Cannabinoids show several neuroprotective properties, acting on several of the main mechanisms leading to cell death after HI: thus, the activation of cannabinoid receptors induce the closure of Ca++ channels, inhibits the transcriptional activity of the Nuclear Factor-κB, reduce cytokine and glutamate release, and modulate the induction of NOS and COX; in addition, cannabinoids are immunomodulators, antioxidants, vasodilators and stimulate neuroproliferation and remyelinization. Some of these effects have been demonstrated in in vivo and in vitro models of HI brain damage in newborn rodents and big mammals as lambs. Regarding the use of cannabinoids for neuroprotection in NHIE, concerns about the possible long term effects of using psychoactive cannabinoids during the perinatal period have prompted some research on neuroprotection by non-psychoactive cannabinoids. In particular, cannabidiol has demonstrated to reduce HI brain damage in in vivo and in vitro models in newborn animals (rodents and piglets), by different mechanisms including anti-oxidation and anti-inflammation as well as reduction of excitotoxicity. Cannabinoïd CB2 as well as adenosine A1 and A2 receptors seem to be involved in some of those effects. In addition, cannabidiol shows some beneficial extracerebral effects in newborn animals. All these properties together with his effectiveness when administered a posteriori to the HI insult, makes cannabidiol an actual candidate for future clinical trials with HI newborns. 

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Cervical insufficiency: The paradigm

Fred K. Lotgering

Nijmegen, NL

Obstetrics has failed to reduce the incidence of preterm delivery. In most cases of threatened preterm labor the cause is unknown, the prediction of true labor inaccurate, and the therapeutic effort little effective.

The various socio-demographic and medical factors associated with preterm birth are associations rather than causes, and often not therapeutically approachable (e.g. race). Whatever the cause, the common pathway of labor is cervical ripening: a complex inflammatory process leading to collagen degradation that allows the cervix to shorten and dilate. The process is enhanced when shortening impairs the immunological barrier of the cervical mucus.

Cervical insufficiency is a working diagnosis. It assumes that in some women the cervix is incapable of carrying a fetus beyond the early third trimester. The natural, classical, history is that of recurrent second trimester loss of a live fetus, following painless dilatation. There is no diagnostic test for it. Cervical insufficiency should not be confused with short cervical length per se or increased burden (twin). The paradigm, or theoretical framework, is that of a pre-existent short or weak cervix (DES, surgery, unknown origin), with concomitant poor immunological barrier that allows ascending bacteria early access to induce cervical ripening and/ or rupture of membranes.

Women with classical history of cervical insufficiency and virtually absent cervix benefit from transabdominal cerclage in 93% of cases. This may be considered proof of concept that operative prevention and/ or treatment of cervical insufficiency is possible. Optimal case selection, surgical technique, and supportive treatment (antibiotics, tocolytics) require further study.
Evidence-based indications and technique for cerclage

Vincenzo Berghella

Philadelphia, USA

Cervical cerclage has been devised in the 1950s. In the last 10 years, several randomized trials have contributed to a much better understanding of the indications for cerclage. History-indicated (prophylactic or elective) cerclage is indicated for women with multiple (usually ≥3) second trimester losses and/or early preterm births. Women with prior preterm births can usually not have history-indicated cerclage, and instead be followed with transvaginal ultrasound cervical length. Ultrasound-indicated cerclage is indicated for women with both a prior preterm birth AND a short cervical length < 25mm between 15-23 weeks. More data is needed to see if it is beneficial in women without a prior preterm birth who develop a short cervix. There is little data to assess the efficacy of physical-exam indicated cerclage, i.e. that cerclage placed because the cervix has been found to be dilated on manual digital exam. One small trial and large cohort studies suggest that is is associated with prevention of preterm birth. Cerclage does not seem indicated in any clinical scenarios if the woman is carrying a multiple gestation. Progesterone and other interventions need to be assessed in high risk women who are candidate for cerclage. Regarding technique, we prefer McDonald cerclage for its ease of placement and removal, as well as its efficacy comparable to Shirodkar cerclage. We use mersilene tape, and try to place as high as possible on the cervix, at least 2cm from the external cervical os.
Operative total cervix occlusion should receive more attention than cerclage

Erich Saling

Berlin, Germany

Early total cervix occlusion (ETCO) is a widespread measure in Germany for cases with recurrent (2) late abortions and early premature births (<32+0gw). Abroad cerclage is used for these purposes, but is a subject of controversy.

As ascending genital infection is the main preventable cause for late abortion and premature birth, a plausible countermeasure is to make an ascension impossible by total occlusion of the cervical canal. Whereas cerclage only tightens the cervical canal, ETCO really closes it: After removing the epithelium of the lower canal and the lower portio these parts are sutured, heal up and thus create a complete barrier.

In our own study and in a multi-center-enquiry the high risk patients had surviving infants in about 70% after Total Cervix Occlusion (TCO). Differentiated according to „early“ TCO (ETCO) and „late“ TCO, the rate has been 80% and 40% respectively. Hormel and Künzel (1995) reported similar Results.

In our group of women treated with ETCO, in 51 previous pregnancies in which cerclage was performed, only 13 infants survived. This is a survival rate of only 26% (as compared to a survival rate of 80% with ETCO).

Due to pathophysiological considerations, namely the prevention of ascending infections by complete closure of the cervical canal, as well as with regard to the disputed benefit of cerclage and the promising Results with ETCO, we think that ETCO should receive more attention in research and clinical practice.

More information: www.saling-institute.org
Inflammatoy markers and selective cervical cerclage

Shigeru Saito, Masatoshi Sakai

Toyama, Japan

Measurement of cervical length in the middle trimester is a promising predictor of risk of preterm birth. Despite cervical cerclage continues to be used routinely, no decisive evidence of its effectiveness has been obtained.

We studied 16,508 women with asymptomatic singleton pregnancy, and measured cervical length and cervical mucus interleukin 8 (IL-8) concentration in the middle trimester. Of these subjects, 252 (1.49%) had a short cervix (25mm). By Kaplan-Meier analysis, the percentages of preterm delivery in cervical shortening and high IL-8 were significantly higher than in those with normal cervical length group (P<0.0001) and normal cervical IL-8 group (P=0.0302). Patients with short cervix were admitted for bed rest, and the attending physician decided whether the cervix should be sutured or not. Overall, risk of preterm delivery in patients with a short cervix did not differ between those undergoing and not undergoing cerclage. However, among patients with a short cervix, those with normal cervical IL-8 were less likely to have preterm delivery if they underwent cerclage.

In contrast, when cervical mucus IL-8 was high, preterm delivery was more likely with than without cerclage. After cervical cerclage, cervical IL-8 levels were rapidly elevated, and these levels two days after operation were significantly negative corrected with the prolongation pregnancy period after operation. These data suggested that we should not perform cervical cerclage to pregnant cases with short cervix and cervical inflammation. With normal cervical mucus IL-8, cerclage for cervical shortening may reduce the rate of preterm delivery.
Cervical occlusion sutures and the role of cervical mucus

Philipp Steer

London, UK

Traditionally, ‘cervical incompetence’ has been diagnosed following the occurrence of painless midtrimester delivery. This is taken to indicate a lack of physical strength in the cervix. Accordingly, cervical sutures have been placed to ‘strengthen’ it. However, as the contribution of inflammation in the onset of labor has become better understood, it is becoming apparent that the role of the cervix is more than acting as a physical barrier. It has active functions to prevent vaginal bacteria ascending into the uterine cavity, which depend on the length of the cervical canal, its diameter throughout its length, and in particular the secretion of mucus which acts to plug the cervix and act as a substrate carrying antibacterial agents such as defensins, lysozymes, lactoferrin, calprotectin, immunoglobulins, and neutrophils. Leucocyte protease inhibitor concentrations in the cervical mucus are more than 1000 times higher than the levels in the fetal membranes. It therefore seems logical to hypothesise that simply to close the cervix physically at a single point (for example, with a McDonald or Shirodkar suture) is likely to be less effective than closing the cervix at either end of the canal. Total cervical occlusion was first documented by Saling et al in 1984, but over the last 10 years we have been using an external os cervical occlusion suture in conjunction with a suture placed close to the internal os to retain as large a cervical mucus plug as possible. We currently await the Results of the prospective randomized controlled trial coordinated from Copenhagen.
Benefits of cervical cerclage in multiple pregnancies

Alexander Strauss

Kiel, Germany

Introduction: As twin- and even more triplet-pregnancies carry an increased risk for preterm delivery, different strategies are used to prolong the pregnancy. This means the clinical implementation of bed rest and hospitalization or the administration of progesterone and/ or tocolytic agents. Furthermore prophylactic surgical occlusion of the cervical canal is scrutinized to reduce the incidence of preterm birth in women pregnant with multiples.

Material and methods: The role of prophylactic cervical cerclage in preventing preterm birth in twin pregnancies is assessed in the available RCT’s. Concerning the small segment of higher order multiple pregnancies conclusions can only be drawn from retrospective data. 16 of 94 triplet-, 9 of 18 quadruplet-/ quintuplet-pregnancies, treated with prophylactic cerclage, were matched to 78, and 9 controls respectively.

Results: In twin pregnancies routine cervical cerclage did not statistically significant alter the incidence of preterm birth, of prelabor rupture of membranes nor of perinatal death. These data from prospective randomized controlled trials (RCT) detect no benefit from routine cervical cerclage concerning twins. In higher order multiple pregnancies gestational age at delivery is not different from the controls for all study groups. Birth weight reveals a dominance of 200g for triplets in the control group, while this significant difference is inverted for quadruplets/ quintuplets (1,245g vs. 1,069g).

With respect to gestational age at birth, the need for hospitalization or for medical intervention is unchanged by surgery. Moreover, perinatal outcome analyzed by arterial pH, APGAR-Score, fetal morbidity and mortality remains equivalent, with or without prophylactic cerclage.

Discussion: The available evidence from meta-analysis of RCT’s in twins and from retrospective observational data in higher order multiples disclaim a positive impact of prophylactic cervical surgery on pregnancy management and/ or perinatal outcome in multifetal pregnancies. Therefore, the routine use of cervical cerclage can not be recommended in all multifetal pregnancies.
Improving patient safety on labor and delivery has become an important goal for hospitals, physicians, patients, and insurers. If we want to make an impact and improve safety, it's not good enough to continue old-fashioned approaches, because they were apparently not effective enough. Significant improvements require changes in physicians' behaviors. The slow progress in implementing patient safety has been blamed on physicians' culture of professional autonomy and the perception by physicians that implementing patient safety measures is a threat to their autonomy and independence.

In 2002, a review of our obstetric professional liability claims found an unacceptably high professional liability payout. In response to this finding, we implemented multiple patient safety features in a stepwise fashion.

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<td>Review of past professional liability experiences</td>
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<td>Labor &amp; delivery team training for all staff</td>
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<td>Chain of command for labor &amp; delivery</td>
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<td>Standardized oxytocin and induction policy</td>
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<td>Magnesium Sulfate/Oxytocin Solutions changes</td>
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<td>Electronic medical record templates</td>
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<td>Changed vacuum to soft cup</td>
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<td>Hire an obstetric patient safety nurse</td>
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<td>Implement an electronic communication whiteboard</td>
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<td>Added 3 physician assistants</td>
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<td>Fetal Monitor Certification; Standardized language</td>
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<td>Post-event meeting with staff and patient if necessary</td>
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<tr>
<td>Drills: Shoulder Dystocia, cesarean section, hemorrhage, maternal arrest</td>
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Results: Our professional liability expenses decreased by 85% for the years 2008 and 2007 as compared to the prior 4 years.
Primary caesarean sections of patients in labor decreased.
Sentinel events decreased to zero in 2008.
Conclusion: Patient safety measures can Result in significant savings within 4 years after it's implementation.
The use of data acquisition system in the resuscitation of the asphyctic newly born infant

Maximo Vento

Valencia, Spain

Survival among infants with birth weight of 500-1,500g in centers of NICHD (USA), was 84% in 1995-6 and 85% in 1997-2002; survival without major neonatal morbidity was unchanged, at 70% between these 2 time periods. New paradigms for addressing care of extremely preterm infants may be necessary to achieve further improvements in outcome. Some of the major morbidities associated with prematurity could potentially be affected by management in the first minutes of life. However, the principles of care which occur in the neonatal intensive care unit are not always utilized in the delivery room. Thus, tools used during newborn resuscitation are generally rudimentary and monitoring is traditionally based on clinical exam alone which can have substantial subjectivity. Therefore we propose:

Applying available technology in the delivery room: a future perspective.
1. High risk pregnancies should be referred to high risk perinatal centers where sufficient number of trained care givers are available around the clock.
2. Every referral center should have at least one DR bed equipped as if it were a NICU bed (“delivery room intensive care unit” or DRICU) to allow titrating FiO2 according to infant’s needs, and continuous monitoring of clinical variables (HR, SpO2, temperature).
3. Ventilation equipment providing CPAP/PEEP and consistent pressure delivery and/or tidal volume monitoring should be used. This may be most effective in the form of a neonatal ventilator or T-piece resuscitator.
4. Data acquisition system to individualize, register and debriefing is essential.

Intensive care of the highest risk newborns begins antenatally and should be continued with equal or greater attention throughout transition, in the DR and into the NICU. Instituting such practices may help achieve further improvements in outcome for the most preterm infants.

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References:
The future of operative vaginal delivery

Klaus Vetter

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In Western countries, risky deliveries are being programmatically abandoned by cesarean sections. This is the consequence of several changes in medicine as well as in our societies, and in our minds, not to say of skills.

Women favor uncomplicated vaginal deliveries in first place, and elective cesareans in second. They dislike emergency cesareans as well as unplanned and possibly traumatic vaginal operative deliveries.

Forceps deliveries were statistically those with most negative consequences for the mother. With less than 1% they meanwhile have become a quantité negligable in Germany. In some places, vacuum deliveries have taken over the 5% – 10% vaginal operative deliveries, in others they changed to the package of secondary cesareans.

Thus, the rise in cesareans is not only a consequence of intensified operative security or of intrauterine acceleration with more babies over 4000g; it is also a consequence of prospective medicine, of the trial to prevent mothers and children from traumatic and emergency deliveries. Nevertheless, forceps and vacuum are not obsolete.
Obstetric pain and its management in the perinatal period: What do we need to know?

Berrin Gunaydin

Ankara, Turkey

A basic overview about the management of obstetric pain in the perinatal period; particularly the practice of neuraxial techniques is addressed. ACOG has stated that in the absence of medical contraindication, maternal request is a sufficient medical indication for pain relief during labor. A focused preanesthetic evaluation including patient’s back examination followed by aspiration prophylaxis and required maternal and fetal monitorization is usually sufficient before neuraxial block in healthy uncomplicated parturients. The choice of a specific neuraxial block is individually based on anesthetic and obstetric risk factors, patient preferences, progress of labor, and resources of the facility. Primary goal is to provide adequate maternal analgesia with minimal motor block by low concentrations of local anesthetics with lipid soluble opioids. Neuraxial analgesia is does not prolong 1st stage of labor or increase rate of caesarean delivery but it is associated with longer 2nd stage of labor and increased chance of instrumental birth. By knowing these facts, laboring parturients can receive neuraxial analgesia when they request. Both epidural and CSE analgesia techniques have been effectively used to initiate analgesia followed by PCEA. A wide variety of infusion regimens with bupivacaine, ropivacaine or levobupivacine plus fentanyl or sufentanil have been described for PCEA. Additionally, offering either single dose or continuous spinal analgesia can be occasionally considered. Currently we prefer CSE analgesia with intrathecal bupivacaine 2.5mg+fentanyl 15 µg followed by PCEA including 0.0625% bupivacaine+fentanyl 2µg/mL (10-15mL/h infusion and 5mL bolus with 10 min lock-out interval and 25-30mL/h limit).
Management of labor pain in the developing world: Defining the benefits

Chandra Susilo

Most women rate pain of childbirth as the most painful experience of their lives. Epidural analgesia is widely considered as the most effective method of providing pain relief during labor. However, in many developing countries epidural analgesia for labor pain may not be routinely available to all laboring parturients for a number of reasons (e.g., economical). Although popular in Europe and North America single dose spinal analgesia for labor pain has not been previously studied in Indonesia. The authors of this report herein present the Results of the first study conducted in Indonesia assessing maternal satisfaction with single dose spinal analgesia (with combination of bupivacaine, morphine, and clonidine) for the management of obstetric pain in Indonesian women. The second goal of this lecture is to review and define the benefits of obstetric anesthesia care in the developing world.
Avoiding complications of obstetrical anesthesia in the perinatal period: An old problem – new solutions

Leon Drobnik

Poznan, Poland

Anesthesia depress nervous system and its regulatory and protective mechanism; general anesthesia - generally, regional anesthesia - in regions of the body, but necessitating involvement of the central adapting mechanisms. Anesthetic inhibition of the compensatory and protective mechanisms are superimposed on physiological changes in pregnancy, optimal for wellbeing of mother and fetus, but elevating the risk of additional injuries.

General anesthesia in parturient is combined with the risk of hypoxia/asphyxia following aspiration of the gastric content, difficulties in endotracheal intubation and after extubation by recovery from anesthesia, due to low functional residual capacity and mucous membranes swelling in pregnancy. Depressive effect of opioids and anesthetics on mother and newborn may cause immediate complications in parturient and neonate and possible remote effects of the disturbed developmental process of the central nervous system.

Education in crisis management, prevention of aspiration and advanced techniques of the instrumental airways protection may lower the risk of perinatal mortality and morbidity.

Regional anesthesia, especially combined spinal-epidural anesthesia is safer option than general anesthesia for delivery of the fetus. Adequate fluid therapy, careful monitoring in the perinatal period, the use of advanced techniques in performing periaxial anesthesia and evaluating neural complications, shall further limit rate of complications in obstetrical anesthesia.

In the years to come, the challenge for the obstetric anesthesia can creates the growing number of parturients with severe cardiovascular or neurologic diseases, as well as drug dependent or obese women. The education and organizational efforts shall be focused on continuous education in crisis management in obstetric anesthesia and perinatal care mother and child. Elaboration and maintaining of the high safety standards in obstetrics, obstetrical anesthesia and perinatal medicine, may diminish further in near future the rate of anesthetic complication.
Perinatal medicine and obstetric anesthesia: Is there a missing link?

Krzysztof M. Kuczkowski

El Paso, USA

The safety of obstetric anesthesia has been debated since its “birth” in 1847, when James Young Simpson (the Scottish obstetrician) first administered “modern” obstetric anesthesia for vaginal delivery. Today obstetric anesthesia has become a recognized subspecialty of anesthesiology and an integral part of practice of most anesthesiologists. Perhaps no other subspecialty of anesthesiology provides more personal gratification than the practice of obstetric anesthesia. An obstetric anesthesiologist has become an essential member of the obstetric care team, who closely works with the obstetrician, midwife, neonatologist and Labor and Delivery nurse to ensure the highest quality care for the parturient and her baby.

Communication skills and exchange of information in ever changing environment of Labor and Delivery is essential for perfect outcome, which is always expected when providing safe passage for both the mother and her fetus from antepartum to postpartum period.

In my early days I could not decide whether I wanted to be an obstetrician or an anesthesiologist. I obtained training in both specialties. Today I get the best of both worlds and there is nothing more challenging and gratifying than the practice of obstetrical anesthesia.
Delivery timing of the growth restricted fetus

Ahmet Baschat

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Fetal growth restriction due to placental dysfunction has important short and long-term impacts that reach all the way into adulthood. Early onset FGR before 34 weeks gestation presents with a characteristic sequence of responses to placental dysfunction that progress from the arterial circulation to the venous system and finally to biophysical abnormalities. In this form of growth restriction safe prolongation of pregnancy is a primary management goal, as gestational age at delivery, birth-weight and iatrogenic premature delivery have important impacts on short term outcome and neurodevelopment. Adjustment of surveillance intervals can be based on umbilical artery and venous Doppler studies. Intervention thresholds need to be based on the balance of fetal versus neonatal risks and therefore critically depend on gestational age. Late onset FGR presents with subtle Doppler and biophysical abnormalities and therefore poses a diagnostic dilemma. Often unrecognized, term FGR contributes to a large proportion of adverse perinatal outcome near term. Adjustment of monitoring intervals should be based on middle cerebral artery Doppler and fetal heart rate parameters. Delivery thresholds can be low. In both forms of fetal growth restriction neurodevelopmental impacts of placental disease occur before management decisions become clinically relevant. This places special emphasis on future preventative studies.
IUGR – postnatal mortality and morbidity

Ludwig A. Gortner

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Background: Intrauterine growth restriction (IUGR) still is a major challenge in perinatal medicine. As to the global view, IUGR in developing countries mostly is secondary to maternal undernutrition, in developed countries, it represents especially in very preterm infants a relative homogeneous group, where most underlying disorders are summarized as placental insufficiency presenting with pregnancy induced hypertension and other related disorders. Most but not all neonates have birth weight below the 10th centile (SGA-neonates).

Results: Neonates born after these pregnancy complications are more likely to develop postnatal pulmonary complications: during the early neonatal period, prolonged times of mechanical ventilation along with an increased risk of bronchopulmonary dysplasia (BPD) have been described nearly uniformly in several studies either from selected or non-selected cohorts. Furthermore, an increased risk of nosocomial infections has been described, potentially affected by prolonged needs for mechanical ventilation and an increased risk of feeding disorders. Neonatal brain damage demonstrated by ultrasound as either intraventricular hemorrhage or periventricular leukomalazia has not been identified to occur more often in preterm neonates, born after intrauterine growth restriction. Mortality has been uniformly found to be increased following IUGR by a factor of 2 - 3 at different levels of gestational age up to term neonates, most studies used as an indicator of IUGR a birth weight below the 10th centile.

Conclusion: Despite several methodological limitations, most studies using SGA as an indicator of IUGR, mortality was uniformly increased compared with neonates without intrauterine growth disorders, pulmonary and infectious complications also were be found to be increased. As impaired intrauterine growth still represents a major challenge for perinatal medicine, continued efforts are mandatory in order to improve outcome in this high-risk group of neonates. Long-term effects further need to be addressed.
Maternal perception of fetal movement: Does it help?

Jan G. Nijhuis

Maastricht, NL

During pregnancy, maternal perception of fetal movements is the first and most important routinely used diagnostic tool. A mother who perceives “normal movements” can be certain that there is no fetal distress. However, severe congenital anomalies can obviously not be excluded by the observation of normal fetal movements.

That decreased fetal movements precedes fetal death is long known, but fetal surveillance techniques seldom includes the mothers perception of fetal movements. Also “kick-charts” have been developed, a simple way of involving the mother in the monitoring of her baby. There is no clear evidence as to how “fetal movements” can best be used in clinical practice.

Fetal movements generally occur in bursts. With increasing gestational age, fetal behavioral states develop, and fetal rest periods up to 45 minutes are not unusual near term. In the counseling of pregnant women, it is important to discuss these changes. Often, the mother may notice that the fetus moves less, while in fact the fetus moves “differently”.

In high risk pregnancies, the decrease of fetal movements may be part of the clinical picture. In those cases, a fetal kick-chart can be used, but thorough instructions of the pregnant woman is crucial. Furthermore, the administration of corticoids for fetal lung maturation has a great influence on the incidence on fetal movements. Whether or not in such cases a kick-chart is used, one needs to be aware of this, and the pregnant woman should be well informed.

In conclusion, information on the fetal activity is an old and inexpensive way to monitor the fetal condition. What the best way is to institute this information in daily care is not precisely established. Within the context of fetal age and the clinical problem, one should realize that “decreased fetal movements” is an alarming signal, which always needs to be further explored
Aortic wall thickness and blood pressure levels in children with intrauterine growth restriction

Erich Cosmi

Italy

Background - Neonates with growth restriction (IUGR) have significant aortic intima-media thickening (aIMT), suggesting that prenatal events might predispose to hypertension. However, beyond the neonatal period, the natural course of aIMT in IUGR people still remains an open question.

Methods and Results - 77 pregnant women were enrolled in this study between January 2006 and June 2007. Their fetuses were classified as AGA (Adequate for Gestational Age) and IUGR if estimated fetal weight was between 10th and 90th or below 10th percentile with Doppler velocimetry abnormalities. Anthropometric parameters and aIMT were detected on each IUGR and AGA fetus at a mean gestational age of 32 weeks. Follow up was performed in 25 IUGR and 25 AGA infants at a postnatal age of 7-to-30 months and same measurements plus blood pressure were performed. Maximum aIMT were significantly higher in IUGR infants than in AGA both in utero (2.05±0.43 vs. 1.05±0.19; p<0.001) and after birth (2.3±0.8 vs. 1.06±0.18; p<0.0001), the Resulting value had a significant correlation (p=0.018). Systolic BP was significantly increased in IUGR subjects (123±16 vs. 104±8.5; p<0.0004) and it was correlated to prenatal and postnatal aIMT values (p<0.0156 and p<0.0054, respectively).

Conclusions - Aortic wall thickening course of IUGR children shows differences with AGA, which may predispose the individual from early life to hypertension and later cardiovascular risk.
Drug use, metabolism and elimination in the very low birth weight (VLBW) newborn

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Drugs are extensively used in sick preterm neonates. More than 400 different drugs are given to sick neonates with about 30 different drugs per baby. Commonly used drugs include antimicrobials such as gentamicin (96%), ampicillin (96%), vancomycin (79%), amphothericin B, diuretics as furosemide (91%) vasopressors (dopamine, dobutamine), opiates (fentanyl, morphine), phenytoin (73%) and others. Duration of therapy varies among drugs. Caffeine is given for 83.3 days (mean), furosemide, 39.8 days, metoclopramide, 73.3 days and chlorothiazide, 74.4 days. Most drugs (>85%) are not approved for use in newborns due to lack of requisite pharmacology data including pharmacokinetics, pharmacodynamics, efficacy and safety. Drug metabolism and plasma clearance are maturationally deficient in neonates and are most pronounced in the VLBW neonates. These physiologic and pharmacologic processes dynamically change with fetal maturity (gestational age) and postnatal age requiring appropriate adjustments in drug dosages. Unfortunately, rational dose regimens based on solid pharmacologic data are severely lacking in neonates which when coupled with the immature organ systems and drug handling capabilities make VLBW neonates extremely vulnerable to adverse drug reactions and drug-induced morbidities and mortality. Thus, VLBW neonates are: 1) subjected to polypharmacy from an immense numbers of drugs; 2) deficient in drug metabolizing enzymes and renal drug excretion; 3) require drug regimens adjusted for gestational and postnatal ages; and 4) extremely vulnerable to drug-induced toxicities. Appropriate pharmacologic studies must be done in VLBW neonates in order to ensure safe, rational and effective drug therapies in this vulnerable population.
Influence of race and gender on outcome at the border of viability

Eduardo Bancalari

Miami, USA

Survival in extremely premature infants has increased as a result of improvements in antenatal and neonatal care. Among the factors that can influence mortality and morbidity in these infants are gender and race. Male preterm infants have an increased mortality as compared to females and also a higher rate of complications such as perinatal asphyxia, RDS, patent ductus arteriosus, infections, bronchopulmonary dysplasia and ROP. They also have a higher incidence of long term neurodevelopmental problems, including CP.

In the USA the rate of prematurity is significantly higher in infants born to black mothers. However, at lower gestations the survival of black infants is better than those born to white mothers. This may be due to a lower incidence of RDS and some of the complications associated with severe respiratory failure.

The advantage of females and black premature infants born at the border of viability is likely due to slightly accelerated fetal maturation but other factors may also play a role.
Birth at the limits of viability: Outcome, ethical and intracultural aspects

Apostolos Papageorgiou

Montréal, Canada

With a dramatic improvement in survival of infants born between 23 and 26 weeks of gestation, survival is not any more a "medical miracle" but a reality that needs to be evaluated with all of its long term potential implications for parents and for society at large. Unfortunately, at the lowest limits of viability, survival is often associated with significant short and long term complications. Hence, it is of paramount importance that extensive consultation between parents and physicians take place prior to delivery. This is possible in the majority of situations. Such consultation can avoid ethical and medico-legal problems. The field of bioethics throughout history has been characterized by occasional tensions between lay persons and physicians relating to the decision making. Bioethics is not only under the influence of medicine but it is also affected by other changing forces such as public opinion, political ideologies, religious beliefs, cultural background and economic conditions. The legal implications of poor communication between parents and physicians cannot be understated. Parental decisions for full medical intervention can widely vary between 23 and 26 weeks of gestation. It is also evident that the physician’s personal beliefs can seriously impact on parental decision. Data presented to the parents on survival and potential complications should reflect local epidemiological information and not general statistics. The prevailing view is that decisions at the limit of viability, when outcome is uncertain or ambiguous, should be the prerogative of the parents. On the other hand, the physician’s responsibility is to protect the life of the infant when unreasonable demands are made by the parents and which do not serve the best interest of the infant. In the final analysis, effective communication between obstetrics, neonatology and parents can prevent conflicts and suffering.
Birth at the limit of viability: How is the German situation?

Christian Poets

Tübingen, Germany

Several countries have developed recommendations to guide decisions on the provision of care for infants born at 22-25 weeks gestational age (wk GA). German guidelines recommend active intervention and treatment for all infants born at ≥24 wk GA; at 22 to 23 weeks GA, the recommendation is to provide treatment at the discretion of the attending neonatologist after counseling the parents, and below 22 wk GA, palliative care only is suggested. These limits are 1-2 wk below those adopted by neighboring countries such as Switzerland and the Netherlands, but do German infants have better outcomes to justify this? To address this question, high-quality outcome data are required. Such data, however, are missing. There are only data from the national quality assurance agency on infants admitted to NICU, showing 25% survival at 22 wk, 47% at 23 wk and 63% at 24 wk, but these data exclude the potentially large proportion of infants who die already in the delivery room. They cannot be utilized as a basis for decisions on treatment policies. There are also data from individual institutions, such as the author’s, including all live-births in 2002-2007 and showing 86% (6/7) survival to hospital discharge at 23 wk and 88% (44/50) at 24 wk; with 42% and 22%, respectively, developing an intraventricular hemorrhage grade III-IV, and 28% and 17% retinopathy grade III or higher. Such single-centre data, however, often show better Results than those from population-based studies and cannot, therefore, be used as a substitute for the latter. Thus, population-based data for German infants born at the limit of viability are needed similar to those gathered by the EPICURE study in the UK or the EPIPAGE study in France. Without such data, the lower GA limit currently in place in Germany can only be regarded as invalidated.
Vaginal birth after CESAREAN SECTION CS: Should it be recommended?

Fabio Facchinetti

Modena, Italy

Vaginal Birth after CS (VBAC) is an health issue that should be evaluated considering both health system organization and socio-cultural context. Therefore, each Obstetric Unit should approach the problem according to local resources and expectancies.

The data present in literature showed that VBAC was successful in 73% of women; maternal morbidity, blood transfusion and hysterectomy were similar in women planning VBAC or elective repeat caesarean section (ERCS), whereas uterine rupture/dehiscence was different (1.3% in VBAC versus 0.4% in ERCS). Maternal morbidity, uterine rupture/dehiscence, blood transfusion and hysterectomy were more common after failed trial of labor (17%, 4.4%, 3%, 0.5%) than after successful VBAC (3.1%, 0.2%, 1.1%, 0.1%) or ERCS (4.3%, 0.4%, 1%, 0.3%). Outcomes were more favorable in successful VBAC than ERCS.

Another recent review valued the balance of risks and benefits of trial of labor versus ERCS and it seems to depend on the risk of emergency CS. Among women with a predicted CS risk of less than 20%, the incidence of uterine rupture was 2.0/1.000 (95%CI 1.1 to 3.2) while among women with CS risk of greater than 40%, the incidence of uterine rupture was 9.1/1.000 (95% CI 6.4 to 12.6), relative risk 4.5 (95% CI 2.6 to 8.1). Therefore women who were at low risk of emergency CS were also at low risk of uterine rupture, including catastrophic rupture leading to perinatal death.

An important reason that lead the management of women with prior CS is attributed to the “physician factor”, meaning that in the presence of comparable obstetrical risk factors, a woman’s risk of receiving another CS is influenced by the practitioner’s attitude and by the institution’s routine. A recent survey on clinicians views on CS explored the opinion on ERCS in 3 different obstetric setting. Obstetrics would offer an ERCS to women with an uncomplicated single pregnancy in cephalic presentation, who had a previous CS for breech presentation in 9% of cases, who had a previous CS for failure to progress in 27% of cases and who had a previous CS for fetal distress in 13% of cases. Professionals’ attitudes and convenience, in addition to cultural issues, have important roles in influencing maternal preferences, requests and outcomes. Women should be accurately informed on the risks and benefits of VBAC. Timing and mode of information are crucial. If adequately counseled, women who request an ERCS may change their opinion in a large proportion of cases, even if doctors do not acknowledge it.
Counseling and caring for pregnant women after a previous caesarean is complex and influenced by numerous factors, including the reason for the first surgery, community and national standards, and women’s choices. Most women considering a vaginal birth after a caesarean section (VBAC) usually have a low transverse uterine scar and are low risk for harmful effects of a trial of labor. Current evidence from several cohort studies suggests that most women and neonates can benefit from a trial of labor and successful vaginal birth after caesarean. Moreover, only a minority experience maternal and neonatal morbidity (e.g. uterine rupture, hysterectomy, need for transfusion, endometritis, NICU). However, because the morbidity can be serious it is important to identify women who are the most appropriate candidates for VBAC. Policies such as “once a caesarean always a caesarean” suggest that all women considering VBAC fall into one category, yet the issues are far more complex. For example, it still remains unanswered whether women who had an elective caesarean section for breech presentation experience different VBAC trajectories from those who underwent caesarean section after a prolonged labor. Should they be classified as nulli- or multiparae for future labors?

This paper will present current scientific evidence to support different strategies for approaching the management of VBAC based on women’s prior labor and birth experiences that resulted in a caesarean delivery. These will include a review of the future potential risks of repeated caesareans for mother and infant and identification of known risk factors related to past labors. Specific suggestions will be made to identify clinical pathways for counseling and care of women and a call for cohort studies across countries to evaluate best VBAC practices.
Sonographic evaluation of the lower uterine segment in patients with previous caesarean delivery

Wolfgang Henrich

Berlin, Germany

Many authors propose a vaginal birth after Caesarean section (CS). The success rate of a vaginal delivery after a CS ranges from 25–77% in the USA and Europe. The rate of a uterine rupture in patients with a vaginal birth after CS is quoted at between 0.007 and 0.43%. Uterine rupture is 17 times more frequent after a CS than in the absence of a previous uterine scar. There is general agreement, however, on the relative safety of the procedure if the clinic meets the criteria required for a surgical intervention.

Several ultrasound studies have been performed to predict the risk of uterine rupture after previous CS. Some authors reported a minimal uterine wall thickness of ≤2mm as an indicator for poor healing of the uterine segment and that a critical myometrial thickness of less than 1.6–2mm, measured by transabdominal US, can identify women at high risk of uterine rupture. Preoperative ultrasound measurements of the lower uterine segment wall thickness correlates well with the true intraoperative situs. This diagnostic tool becomes increasingly popular.

There seems to be a relevant variability of measurements depending on bladder filling, uterine tone, leading part of the fetus and compression of the lower uterine segment due to fetal structures. This variability might be one of the explanations for discordance between preoperative ultrasound and intraoperative findings.

So far, there is no agreement or standard about where, when and how to measure the lower uterine segment sonographically. However, dehiscent or paper-thin segments are detectable by combined transabdominal and transvaginal ultrasound and, on clinical grounds, have diagnostic relevance to diagnose imminent uterine ruptures.
Limitations in current management of labor

Dan Farine

Toronto, Canada

The human fingers are limited in assessing fetal head station, position, and cervical dilation. Fetal Head Station: Assessing station was examined using a pelvic model simulation. The clinicians failed to identify station in 36-80% of cases. Even when exact station was disregarded and the station was labeled as high, mid, or low, incorrect diagnosis occurred in 34% of assessments. Furthermore, care givers in labor seem to disagree on the definition of station.

Fetal head position: The fetal head position using digital examination can be easily compared to the position determined with ultrasonic imaging. Two studies showed that clinical assessment of fetal head position was correct is only 40-55% of cases. In one of these studies it was assessed that forceps could have been applied incorrectly in 25%.

Cervical dilatation: Studies comparing two examiners showed a variability of 1-2cm in the assessment of the vaginal examination, although it may reach up to 6 centimeters. Studies with cervical models showed that the accuracy of clinicians in assessing cervical dilatation within 1cm was only about 50%.

Previous attempts at cervicometry: A variety of mechanical, electromechanical, electromagnetic and ultrasound based cervicometers have been developed by many researchers in the last 50 years. However, none gained clinical acceptance. Van Dessel and Lucidi had excellent reviews on the topic. Alternative methods trying to assess these parameters indirectly were also not successful.

This session is dedicated to three different and novel approached to overcome these problems.
Can we visually assess labor progress?

Dorit Hochner

Jerusalem, Israel

Introduction: Monitoring of birth progress has traditionally been performed by midwives and obstetricians by manual examination. This method of repeated digital examinations is, however, intrusive, potentially dangerous, associated with the risk of ascending infections, inaccurate and, causes significant discomfort to the laboring mother.

Aim: To develop an alternative method to monitor birth progress while overcoming the disadvantages of manual examination.

Method: We developed an integrated-technology device for the continuous real-time monitoring of labor progression, including cervical effacement and dilatation, fetal head position and fetal heart rate. The innovative technology offers delivery room healthcare professionals the first multi-parameter labor-monitor that not only enables accurate, real-time data acquisition and recording without the need for constant staff intervention, but also allows the mother in labor to move around freely in the vicinity of the labor ward.

The device was assessed in 53 birthing mothers in the labor ward of Hadassah Mount Scopus, Jerusalem, and maternal and neonatal outcomes were compared to that of a similar number of matched controls.

Results:
A) The device was found to be feasible and accurate in monitoring labor progression, demonstrating cervical effacement and dilatation, fetal head station and fetal heart rate as compared with traditional labor monitoring.
B) The method was found to be comfortable for the laboring women both while reclining and during ambulation.
C) No significant differences were found between the study and control groups in the course of labor, complications or infections during or after birth, nor in neonatal outcomes.

Conclusions:
1) We have succeeded in developing a reliable device that offers an innovative alternative method to monitor the progress of labor.
2) We are currently working to expand monitored parameters to include intrapartum fetal acid-base balance.
The laborpro solution – non-invasive ultrasound based determination of labor parameters

Yoav Paltiel

Haifa, Israel

Introduction: An accumulating body of literature suggests that ultrasound can play an important role in the objective determination of station and position during labor. The FDA cleared LaborPro system (Trig Medical Inc.) allows non-invasive and objective determination of labor parameters using ultrasound imaging and a position tracking system. The LaborPro main features include:

- Automatic measurements of head station and position, and head descent during contractions. By marking known ultrasound landmarks (e.g. BPD, head tip, orbits) on screen, the LaborPro system calculates the spatial position of the fetal head relative to pelvic inlet plane and birth canal.
- Non-radiating Pelvimetry. 3D pelvic mapping is performed by using position sensors and ultrasound to simply mark known landmarks of the maternal pelvis.
- Determination of cervical dilatation and length. By attaching a miniaturized sensor to the examiner’s finger, the system enables objective assessment of cervical dilatation and length.

Clinical data: Several large multicenter studies (US, Israel, and France), using the LaborPro system were performed. Comparison of vaginal examination with the system head station results revealed a mean absolute difference of 5.5mm. Vaginal examination head-position evaluation, within a 45-degree interval, complied with the system in only 40% of the measurements.

Our data show that when fetal head is engaged as defined by the LaborPro system, the cervix is fully dilated in 80% of cases and there is a remaining risk of caesarean section of 1.6%, but not for non-progressive labor.

Evaluation of the accuracy of clinical measurement of cervical dilatation with the LaborPro during vaginal examination shows limited precision.

Conclusion: Our data show that the LaborPro’s ultrasound-based, non-invasive technology can accurately determine all labor progression parameters. The system might contribute to the decision-making of the medical staff especially in cases of non-progressive labor and operative deliveries, and to patient’s safety and comfort.
Birchtrack: An ultrasound based computerized labor monitoring system

Barak Rosenn

New York, USA

Nowadays, as in the distant past, digital vaginal examination remains the means by which to determine cervical dilation and fetal head station to assess progress of labor. The vaginal examination, however, is inaccurate, non-contiguous, increases the risk of infection, and is associated with maternal discomfort. Estimations of cervical dilatation by different care providers vary by more than 50% and disagreement by more than 1cm is quite common. Furthermore, assessing progress of labor can only be done in a retrospective fashion, comparing cervical dilation and head station at a given time to the information obtained during the previous examination. Real time detection of abnormal labor patterns could potentially allow the provider to intervene earlier and modify management accordingly.

Birchtrack is a computerized labor monitoring system that provides continuous real time data on cervical dilation and fetal head station. The system measures cervical dilatation using three external ultrasound transducers located on the maternal abdomen, and two internal transducers attached to each side of the cervix and calculating the distance between the two internal transducers via triangulation. Another transducer attached to the fetal scalp is used to calculate head station and to monitor the fetal heart rate.

In more than 400 deliveries studied using Birchtrack, there were no instances of infection or bleeding related to the system and maternal satisfaction was high. The system provided information on progress of labor with a high degree of reliability. Additionally, it provided a method to gauge the effect of individual contractions on cervical dilation and head station.

The Birchtrack system has the potential to improve the efficacy and safety of managing labor, to increase patient satisfaction and provider convenience, and to reduce the overall cost of delivery.
Neonatal morbidity associated with chorioamnionitis in premature under 1,500g

Xavier Carbonell Estrany

Barcelona, Spain

Respiratory distress syndrome (RDS), neurological damage (intraventricular haemorrhage (HIV), periventricular leukomalacia LPV, cerebral palsy (CP)), sepsis, poor neurological outcome and increased rate of perinatal deaths have been related to the presence of Chorioamnionitis (CA). Chorioamnionitis activates the inflammatory pathway and the biochemical mediators would be associated with the premature labour and may cause the possible damage of the foetus and newborn infant. These mediators could be found in other situations: premature rupture of membranes (PROM) and premature labour, which can be confounding factors.

To find out if there is any correlation between maternal clinical chorioamnionitis and acute morbidity and mortality in premature newborn infants, a multicentre prospective case-control study was designed with premature infants ≤ 1500g matched by gestational age. There were 165 cases and 163 controls. A significantly higher percentage of cases than controls required intubation (53% vs. 35.8%), had normal intrauterine growth (98.1% vs. 84.7%), were born in the tertiary centre (inborn) (95.1% vs. 89.1%), from single gestations (76.4% vs. 65.6%) and vaginal delivery (47.3% vs. 33.3%), showed a lower Apgar score at 5 min, and presented a higher rate of early-onset sepsis (10.4% vs. 1.2%). Older maternal age (32.5 vs. 30.8 years), premature labour (67.3% vs 25.8%), premature rupture of membranes (61.3% vs. 25.8%), and antibiotic treatment (88.5% vs 52.3%) were significantly more frequent among cases than controls.

Follow up during 2 years is being performed in both groups to compare neuropsychological development.

In summary if gestational age is controlled, chorioamnionitis is associated with neonatal depression and early sepsis but not with other complications of the prematurity.
Mechanisms of infection-associated preterm labor: Influences of fetal sex

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Preterm birth is clearly recognized as a syndrome characterized by different pathophysiologic pathways which have a temporal dependency. Stress pathways involving activation of the maternal and/or fetal hypothalamic-pituitary adrenal axis appear to predominate later in gestation whereas preterm birth associated with inflammation or infection has a higher incidence earlier in gestation. The infection-driven pathway involves up-regulation of the prostaglandin-cytokine cascade, and we have recently shown suppression of key steps in this pathway by probiotic lactobacilli GR-1 supernatant. It has been reported that the incidence of preterm birth, and preeclampsia are higher in pregnancies carrying a male fetus. We found that effects of lipopolysaccharide (LPS) on placental trophoblast cells from pregnancies carrying a male fetus were greater than cells carrying a female fetus and this correlated with enhanced expression of prostaglandin synthase-2 enzyme. Conversely, expression of the prostaglandin metabolizing enzyme (PGDH) and the anti-inflammatory cytokine (GCSF) was greater in cells from pregnancies carrying a female fetus. While this information suggests the mechanism of a gender-associated effect on the incidence of preterm birth, the impact of other factors on these pathways and the temporal dependence of the gender-related incidence of preterm birth requires further elucidation.
Antibiotics for the prevention of preterm birth

Ronald F. Lamont

Lamont, UK

The ORACLE study, its seven year follow up, the meta-analyzes and systematic reviews which include it, together with a number of editorials and commentaries, often suggest that antibiotics used to prevent preterm birth (PTB) are ineffective and may cause more harm than good. This conclusion is incomplete. A more accurate conclusion would be that the use of erythromycin or co-amoxiclav, or both, given to women in threatened preterm labor (PTL) with intact membranes, without evidence of infection as a cause of the PTL, may decimate normal genital tract flora late in pregnancy and therefore cause more harm than good for the following reasons:

a) Erythromycin and co-amoxiclav are ineffective against those organisms (bacterial vaginosis [BV] and its related organisms) known to be associated with PTL and PTB.

b) It is a self fulfilling prophecy that antibiotics would be ineffective under such circumstances since those women who were in genuine PTL which led to PTB were not infected (no objective evidence of abnormal colonization was sought; women with clinical infection were excluded from the study; by the investigators own estimate, only 13-22% of participants had what they considered sub-clinical infection).

c) The antibiotics were administered at a time in pregnancy when the inflammatory cascade which constitutes the labor process will have resulted in irreversible changes in the cervix and myometrium.

In contrast, a number of studies using an antibiotic active against BV or BV revealed organisms (clindamycin) given to women with objective evidence of abnormal genital tract colonization (BV on gram stain), early in pregnancy, before infection and inflammation have caused irreversible damage, (the majority of women were treated before 20 weeks gestation) have demonstrated a 40-60% reduction in the incidence of PTB. Less harm will be done by correcting abnormal colonization in early pregnancy than by causing decimation of normal flora late in pregnancy.

Nevertheless, the long term effects of antibiotics remains unknown and the use of antibiotics in pregnancy should be strictly monitored.
Perinatal antibiotics and nosocomial infections in very low birth weight infants

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The reduction of neonatal group B streptococcal early-onset infections by intrapartum antibiotics and the association between chorioamnionitis and cerebral palsy in preterm infants have increased the popularity of administration of antibiotics to pregnant women with preterm labor, as well as to preterm infants born after preterm labor. There are, however, points of concern:

1. Prepartum antibiotics are effective against group B streptococcal bacteremia but there is no evidence for an effect of antibiotics given prior to delivery on gram-negative or enterococcal bacteremia (Gilbert-RE BJOG 2005)
2. In preterm infants, rates of infections with gram-negative enterobacteriaceae increase alongside increased prepartum administration of ampicillin (Bizzarro-MJ Pediatrics 2008)
3. In preterm infants, there is an emergence of infections with gram-negative enterobacteriaceae resistant to ampicillin alongside increased prepartum administration of ampicillin (Bizzarro-MJ Pediatrics 2008)
5. Prolonged duration of empirical antibiotics after birth is associated with increased rates of necrotizing enterocolitis or death (Cotton-CM Pediatrics 2009)
7. Antibiotics given to women with preterm labor may increase the risks cerebral palsy and functional impairment of children assessed at school age (Kenyon-SL, Lancet 2008)

These data call for the judiciously restricted use of antibiotics both in women with preterm labor and in infants born preterm.
In utero influence of a male on its female co-twin: Perinatal and long-term implications

Isaac Blickstein

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The classical 'twin method' looked for more than 100 years on the relative influence of Nature vs. Nurture in MZ twins. Certainly, sharing of the same placenta (and circulation) in the MC subtype is evidence of in utero influence of one twin on its co-twin. In contrast, unlike-sexed twins were considered as merely being two distinct fetuses that just happen to share the same uterine cavity. In the last decade, several studies suggested that an in utero influence of a male on its female co-twin might exist. This was supported, although not universally, by finding of larger females in male-female compared to female-female pairs. In addition, neonatal respiratory morbidity of females from unlike sexed pairs is more similar to that of male infants. These observations lead to the hypothesis that a substance might exist which is transferred from the male to the female in utero and is responsible for this programming event. The idea is also supported by animal models and by observations that females from female-female sets are significantly different than those from male-female sets in terms of adolescent gynecological morbidity, infertility, marriage pattern, early menopause, and breast cancer. At present, neither the nature of the substance (paracrine or endocrine) nor the way of transfer (intra- or extra-uterine) are known. Despite the speculative characteristics of the observations, the unlike-sexed twins seem to rightfully become the focus of extensive research.
Multiple pregnancy and delivery

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During the last decades the rate of multiple births increased in our population from 9.3 to 12.5‰ mostly because of wide implementation of assisted reproduction technologies. Despite of recent improvements in obstetric maternal care, monitoring of fetal well-being and neonatal intensive care maternal, fetal and neonatal outcome is much more favorable in singleton than in multiple pregnancies.

The problem of preterm birth is one of the most important in multiple pregnancy care that depending on not only from the pregnancy complication but from medical iatrogenic causes as well. 10 times higher rate of preterm birth in multiple pregnancy population then in singleton one leads to increase of perinatal mortality and perinatal morbidity rates.

Timing of delivery and the optimal route of delivery in multiple pregnancy are still very controversies. There are factors influence on the decision making process – one of them is “premium pregnancies and premium fetuses and neonates” status those quite often are the cause of 45% of preterm deliveries and 58% of caesarean deliveries in the population. This influence is very clear in privet clinics were the rate of caesarean section in multiple pregnancies aspires to 100%. Elective caesarean with out of clear obstetrics or fetal indication leads to increase of neonatal asphyxia rate.

The fetuses presentation influence on the mode of delivery and after TBT is hardly support vaginal birth in doctors population. But not only our data that rate of asphyxia at birth in second twin in vertex-breech after caesarean is higher than after vaginal deliveries should to be taken into consideration in the decision making planning in multiple pregnancy care. The idea is not to reduce of caesarean section rate in multiple pregnancies but reduce the rate unnecessary caesarean delivery.
Neonatal mycoplasma hominis (Mh) or ureaplasma urealyticum (Uu) colonization and neurological outcome in very preterm infants

Yannick Aujard

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Vaginal colonization of Uu/Mh in pregnant women is a major risk factor for perinatal infection and preterm delivery (Sanchez, 1990). It could induce amniotic membranes inflammation leading to subsequent chorioamnionitis (ChA) increasing the risk of intraventricular haemorrhage (IVH) and white matter damage (IN Olumu, 2009; L Kirchner, 2009).

We conducted a retrospective case-control study to evaluate the consequences of Uu / Mh airway colonization on neurological development in very premature infants. Neonatal events and follow up at 2 years of age of a cohort of preterm infants born below 32 weeks’ gestational age with Uu/Mh colonization >104cfu/ml were analyzed. Fifty-nine consecutive cases treated with an oral macrolide were compared with 118 controls, not colonized. Results: A clinical ChA (27%) and a prolonged rupture of the membranes (47%) were usually associated with postnatal Uu/Mh airway colonization. Early neonatal morbidity was not worsened by Uu/Mh colonization. Neurological investigations (EEG, ultrasound scans) did not show any deleterious effect of Uu/Mh compared with controls. The neurological follow-up at 6 months, 1 and 2 years of age did not show any difference between the colonized treated and control groups.

Despite agreement on the deleterious effects of Uu/Mh on ChA and bronchopulmonary dysplasia, conflicting data are reported on the impact of Uu alone or associated with bacteria on the increased incidence of IVH grades 3 and 4, ventriculomegaly, echolucent-and echodense cerebral lesions. New data on animal models (E Normann et al, 2009) and the role of prenatal antiinfectious therapy (R Roero, 1992; MMazor, 1993) will be discussed.
Neurodevelopmental outcome of extremely preterm infants

Manuel Carrapato

St Maria da Feira, Portugal

In our institution we report survival rates of 56.4% at <26 weeks GA. Survival is not the only goal when attempting to establish a ‘lower limit of viability’. Outcome and quality of life is a major priority, as neuro/psychomotor, neurosensory, cognitive disfunctions are found especially in the most immature infants, <25 gestational weeks. Our data shows that at school entry, very preterm babies <32 weeks gestation, 6.1% presented with moderate to severe CP, whilst minor neurologic abnormalities were found in 50%. Visual impairments were present in 24%. No blindness or deafness were registered.

Learning disabilities, behavioral problems and ADHD were found in 58%, 36% and 15% respectively. It is quite plausible that some of the adverse outcome in survivors at these low gestational ages may not be just the direct effect of prematurity and/or low birth-weight per se but also the Result of the hostile intrauterine milieu leading to preterm delivery from inflammatory mediators, to IUGR, hypoxic-ischaemic insults, metabolic imbalances, etc. Postnatal events, from nosocomial infection to anaemia and haemodynamic instability, metabolic derangements of hyper/hypoglycaemia and electrolytic disturbances, etc. may also play an adjuvant role in the overall picture of survival with multiple handicaps. But one area in particular should call for special caution: the possible role of iacterogenically-induced disability.

These sequelae and complications of surviving ELBW infants at the threshold of viability place an enormous responsibility upon society as a whole, particularly for the allocation of financial and human resources to provide the necessary collateral help. How sensitive are we to handle their multitude of needs and how prepared are we to integrate them into society with fairness and equity? So far the approach and emphasis has been on survival, psychomotor disability, cognitive learning and behavioral problems. The long-term adult metabolic syndrome is another concern only now surfacing.
Survival rates have improved dramatically in recent years for extremely preterm infants. However, they remain at significant risk for a wide array of long-term morbidities, which are mostly inversely related to gestational age. Cerebral palsy occurs in 10-15% of very preterm survivors, at rates 50-75 times higher than in term children. Major neurodevelopmental disability, comprising any of moderate or severe cerebral palsy, blindness, deafness, or developmental delay (DQ scores more than 2 SD below the mean for controls) occurs in approximately 1 in 4 extremely preterm survivors, compared with 1-in-25 term controls. However, with the introduction of therapies shown to reduce cerebral palsy, such as caffeine for apnoea of prematurity, the rates of cerebral palsy and major neurosensory disability may be expected to fall. Later in childhood, other neurodevelopmental disabilities become more apparent, interfering with schooling, and persist into adolescence. Extremely preterm survivors have IQ scores ⅔ - 1 SD below those for controls. They also perform significantly worse on tests of reading, spelling and arithmetic, and they have more attentional difficulties, internalizing behaviour problems, and immature adaptive skills. Assessment of executive function reveals more problems compared with controls in all areas assessed, and more have developmental coordination disorder than controls. Although survival rates for the most immature infants have increased dramatically with improvements in perinatal and neonatal intensive care in the last 20-30 years, long-term neurodevelopmental morbidity rates remain high, and have ongoing health consequences throughout childhood.
Noninvasive assessment of prenatal neurodevelopment using fetal magnetoencephalography

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The maturation of the human neuronal functions takes place during the last month of gestation and the first 3 months of life. But currently there are no reliable tests to assess functional integrity of the fetal brain directly. Fetal magnetoencephalography (fMEG) by using auditory or visual evoked response could be a viable non-invasive method to detect the prenatal functional maturation process. Until now the very low signal-to-noise ratio is the main problem, because the expected fetal neuronal signal strength lies below 100fT and is superposed by the 10- to 100-fold stronger magnetic fields of the maternal and the fetal heart. The earliest successful recording of a cortical auditory evoked response (CAER) component was performed at week 27 with an observed peak latency of 294 ms. Several different components could be differentiated in the CAER complex and in all detection rate is 77 %. The development of the fetal CAER show a negative correlation of their peak latencies with increasing gestational age in normal, but not growth restricted fetuses. The results are in good accordance with EEG studies in preterm neonates. In a clinical study fMEG has proven viable to elucidate cerebral side effects of antenatal steroid therapy. So fMEG allows to observe the development of a parameter of prenatal cortical function that can be interpreted as maturation.
Patent ductus arteriosus and lung injury in the premature infant

Eduardo Bancalari

Miami, USA

A persistent ductus arteriosus is a common event in small preterm infants. The systemic-to-pulmonary shunting and increased pulmonary blood flow that occurs as the pulmonary vascular resistance decreases after birth can have significant cardiovascular and respiratory consequences. Pulmonary effects include pulmonary edema and hemorrhage, worsened lung mechanics and deterioration in gas exchange with hypoxemia and hypercapnia. The increased pulmonary blood flow can also produce damage to the capillary endothelium and trigger an inflammatory cascade. This, plus the need for longer and more aggressive mechanical ventilation, can explain the association between a prolonged patent ductus arteriosus and an increased risk for bronchopulmonary dysplasia. Recent evidence from an animal model of BPD suggest that a persistent ductus arteriosus also may decrease alveolar septae formation leading to histological changes similar to those found in BPD.
Are there strategies to prevent or treat bronchopulmonary dysplasia (BPD)?

Christian P. Speer

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Many strategies to prevent or ameliorate BPD have been evaluated so far. Evidence for a short term preventive effect exists for the repetitive intramuscular administration of high doses of vitamin A. Oxygen supplementation remains an important therapeutic strategy for patients with established BPD. Targeting the infants at lower oxygen saturation seems to reduce long term pulmonary morbidity without increasing the risk of adverse neurosensory outcome. In addition, prophylactic or very early surfactant administration in very immature infants may have a beneficial effect on the incidence of BPD. Currently there is no sufficient evidence for a routine use of inhaled nitric oxide (iNO) for the prevention of BPD. A temporary use of diuretics can improve lung function and oxygenation in these infants. Nonetheless existing data do not justify a sustained diuretic therapy.

As the pathogenesis of BPD is multifactorial, it is unlikely that one single agent will be identified as a ‘miracle drug’ in the prevention or treatment of the disease. The ‘miracle drug’ of the 1990s, dexamethasone, has almost completely lost its role in the management of extremely premature infants. Superoxide dismutase (SOD) and 1-Proteinaseinhibitor have not proved to reduce the risk of moderate or severe BPD yet. Effects of other anti-inflammatory substances still have to be assessed in detail. The early administration of caffeine for prophylaxis and treatment of apnea of prematurity has been shown to reduce the risk of BPD and to improve the rate of survival without neurodevelopmental disability at follow-up.
Ureaplasma associated bronchopulmonary dysplasia: Can it be prevented?

Leonard E. Weisman

Houston, USA

Ureaplasma is the single most common microorganism isolated from the lower respiratory tract of newborn infants, and is associated with neonatal pneumonia and bronchopulmonary dysplasia. Erythromycin has been suggested as the drug of choice to treat or prevent Ureaplasma associated lung disease. However, erythromycin has failed to prevent infection in 17 studies (8), and erythromycin treatment has failed in 5 studies. We are currently observing that more than 74% of Ureaplasma in the perinatal period is resistant to erythromycin and 100% appear sensitive to azithromycin. In a neonatal animal model of Ureaplasma and oxygen induced lung disease, appropriate antibiotic prophylaxis (erythromycin versus azithromycin) improved survival and morbidity, and decreased lung inflammation. Ballard et al, however, recently reported that prophylaxis or early treatment of Ureaplasma, in preterm infants with birth weight <1,250 grams, with azithromycin did not affect survival and or incidence of bronchopulmonary dysplasia, but appeared safe. In both of these studies, the dose of azithromycin was 10mg/kg for 7 days then 5mg/kg for a maximum of 6 weeks, and dosing was based on clinical practice not pharmacokinetics. In our neonatal mouse model of Ureaplasma and oxygen induced lung disease, azithromycin pharmacokinetics appears to impact the outcome. Specifically, azithromycin prophylaxis survival is dose related and correlates directly with serum or lung tissue levels. Thus, more effective strategies to prevent Ureaplasma related lung disease may improve clinical outcome. These strategies should include: 1) early identification of infected neonates, 2) determination of organism sensitivity in-vitro, 3) selection of appropriate antibiotic and dosing scheme. Previous attempts to prevent or treat Ureaplasma related pneumonia and bronchopulmonary disease in neonates appeared to fail because of inappropriate antibiotic or dose. Pharmacokinetic, safety and efficacy studies of azithromycin prophylaxis in at risk neonates are needed.
3D sonography of the fetal midline supratentorial anomalies

Vincenzo D’Addario

Bari, Italy

Three-dimensional ultrasound is the most innovating and attracting modality in the field of ultrasound imaging and represents a superb tool to perform an accurate fetal neuroscan. Once the fetal brain has been scanned, it is then possible to “navigate” in the stored volume choosing among the multiple scanning planes on the three orthogonal spatial axes. Last generation 3D equipments have multiple software facilities which are extremely useful to correctly evaluate the fetal brain such as the multiplanar view, the tomographic ultrasound imaging (TUI), the volume contrast imaging in the C plane (VCI-C plane). Thanks to these imaging modalities it is possible evaluate the finest anatomical details of the developing brain and to increase the diagnostic accuracy when an abnormal sonographic finding of the fetal brain is recognized during the routine examination.

The two fundamental landmarks in the brain anatomy, which both can be easily seen with the reported 3D facilities are: the corpus callosum and the cerebellar vermis. The evaluation of the corpus callosum is useful in the differential diagnosis of different supratentorial anomalies. Complete or partial agenesis of the corpus callosum are present in multiple cerebral congenital diseases frequently associated with ventriculomegaly. Furthermore the visualization of the corpus callosum is useful in the correct diagnosis of other disorders of prosencephalic development such as absent septum pellucidum, septo-optic dysplasia and lobar holoprosencephaly, as well as the correct location of abnormal midline cystic lesions, such as velum interpositum cyst and arachnoid cysts.
4D sonography in functional evaluation of fetal brain

Asim Kurjak

Zagreb, Croatia

Understanding the structure and function of the fetal nervous system has been the dream of physicians for centuries. The pioneering efforts of Ian Donald in obstetric ultrasound in the latter part of the twentieth century have permitted this dream to become a reality. The initial contribution of obstetric ultrasound focused on normal and abnormal structure. Initially, anencephaly was described and followed by increasingly subtle central nervous system abnormalities such as agenesis of the corpus callosum.

The current and evolving challenge for investigators in obstetric ultrasound is to have similar success with the understanding of fetal neurological function. There are many functional neurological abnormalities such as cerebral palsy whose causes are poorly understood. This uncertainty regarding causation vitalizes plaintiff's attorneys in the United States and increasingly throughout the world who attempt to relate these neurological abnormalities exclusively to intrapartum events such as usage of oxytocin, forceps deliveries and failure to perform a Cesarean delivery. While there are some cases where causation is probably related to such intrapartum events, this is usually not the case.

An evolving challenge for the medical profession is to better define normal and abnormal fetal neurological function in utero so that we can better predict antenatally which fetuses are at risk for adverse neurological outcomes irrespective of intrapartum management.

A new prenatal scoring test has been introduced and evaluated in four centers in high risk pregnancies. It might have good potential in the assessment of integrity of fetal CNS.
Does 3D/4D obstetrical sonography improve perinatal outcome?

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Mineola, USA

Objective: The purpose of this presentation is to review the literature on 3D/4D obstetrical ultrasound in order to determine its clinical usefulness.

Study Design: The literature review included articles written in English published from 1993 to 2008. PubMed was used as the search engine and original articles, case reports, review articles (and references from review articles) were included. Each article was assessed for relevance and the level of evidence was determined by two different individuals. The main outcomes of interest included: maternal and perinatal mortality and morbidity, maternal-fetal bonding, cost-effectiveness and possible side-effects. The review will be updated in September 2009.

Results: A total of 145 relevant articles were identified; 90 (62%) were pure descriptive, 40 (27%) were diagnostic comparing 3D/4D vs. 2D ultrasound, 7 (5%) were outcomes-based comparing 3D/4D vs. 2D ultrasound and 8 (6%) were review articles. Most articles 124 or 86%) were published in year 2000 or later. As compared to 2D ultrasound, 3D/4D ultrasound increased the detection rate of cleft palate and the diagnostic information (not detection rate) of some other facial abnormalities, neural tube defects and limb/skeletal abnormalities. No evidence of improvement for any of the examined obstetrical outcomes was found. In contrast, it appears that the cost of care is being increased considerably by 3D/4D obstetrical ultrasound.

Conclusion: The improved diagnostic information by 3D/4D ultrasound has the potential to lead to better outcomes. However, additional research is needed to determine its clinical usefulness.
Sonographic imaging of the posterior fossa

Yaron Zalel

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Agenesis of the cerebellar vermis is an uncommon defect, and it is usually detected while evaluating the posterior fossa. It could be as part of the DWM or as an isolated finding. It could also present as complete agenesis or partial, i.e. inferior vermian agenesis. It may be impossible to correctly diagnose antenatally a defect in the cerebellar vermis in all cases. A very high proportion of disagreement was found between prenatal ultrasonic diagnosis of Dandy-Walker malformation or variant and autopsy findings, emphasizing the need in accurate sonographic demonstration of the cerebellar vermis.

The purpose of our presentation is to evaluate the posterior fossa of the fetal brain.

It is emphasized, that the diagnosis of vermian agenesis (especially partial agenesis) cannot be made prior to 18 weeks of gestation!!

Detailed US of the posterior fossa should include not only the measurements of the vermis, but also the structure of the vermis (primary fissure, fastigium), but also the relationship to the cisterna magna, the 4th ventricle, the tentorium as well as to the pons.

Enlargement of the posterior fossa - Is it always pathological??

It depends on the gestational age. Also, the possibility of rotation of the vermis should be included in the differential diagnosis. The demonstration of the normal vermis on mid-sagittal plane in cases with enlarged cisterna magna on standard plane raises the possibility of rotation of the vermis.

When comparing ultrasound to MRI of the fetal posterior fossa, it is sometimes easier to perform a perfect midline sagittal slice with US than with MRI before 25 weeks. Early MRI adds little new information compared with well-conducted US.

The contribution of 3D-US to the sonographic demonstration of the posterior fossa is emphasized.
Pathophysiology of hemorrhagic shock

Wayne Roy Cohen

Bronx, USA

Hypovolemic shock is characterized by inadequate blood flow to vital organs. The Result is insufficient oxygen for metabolic needs, causing release of inflammatory mediators, endothelial dysfunction, and disruption of normal metabolism. With hemorrhage, oxygen delivery falls because of decreased cardiac output and hemoglobin concentration. Compensatory mechanisms initially maintain sufficient oxygen delivery to sustain oxygen consumption. With continuing blood loss a critical point is reached beyond which further fall in oxygen delivery causes a commensurate drop in tissue oxygen availability. At this juncture the patient will deteriorate very rapidly.

As blood is lost, sympathoadrenal activity increases in an attempt to maintain cardiac output and, as output falls, to defend the blood pressure. Blood pressure can remain adequate for some time in the face of hemorrhage and falling cardiac output. Anxiety, restlessness and diaphoresis are manifestations of catecholamine effects. The Resulting selective increase in vascular resistance redistributes cardiac output to maintain oxygen delivery to vital tissues. This is why bleeding patients have tachycardia and pale cool skin, and why arterial pressure does not always reflect global tissue perfusion.

As hemorrhage worsens, stroke volume and blood pressure fall. Heart rate continues to rise in an attempt to maintain cardiac output but eventually all of these adaptive responses fail and the effects of circulating vasodilating substances supervene.

Cellular changes begin early in blood loss. Membrane polarization changes lead to ion pump dysfunction. Water moves rapidly into cells, inhibiting microvascular perfusion, and contributing to development of acidosis. These membrane changes begin before systemic hypotension and can be reversed early in the process by improving tissue perfusion and replacing extracellular fluid.

In ischemic tissue an inflammatory response leads eventually to multiple organ dysfunction syndrome. Changes in lung performance are common. Myocardial function is impaired. Low blood pressure reduces coronary perfusion and inhibits contractility. This diminishes flow in the microcirculation, leading to platelet aggregation and small vessel clots. Local hypoxia increases capillary permeability and intravascular fluid is lost, further compromising preload and coronary artery flow.

In late shock central vasomotor control centers fail; diffuse vasodilatation occurs. Acidosis becomes profound and causes further deterioration of basic metabolic functions. Ischemia and reperfusion compromise integrity of the gut wall and bacterial toxins escape into the circulation, feeding the multi-organ dysfunction that is developing.
PPH: Conservative management of placenta accreta

Wolfgang Henrich

Berlin, Germany

Depending on the depth of invasion, distinction is made between placenta accreta, increta or percreta (up to the serosa or even exceeding the uterine wall). The prevalence is increasing due to a rising rate of c-sections. 20% of cases are associated with placenta previa. Predisposing factors are previous Caesarean section (CS), curettage, endometritis, myomectomy and retained placenta in a previous pregnancy. Sonographic features are placental lacunae with turbulent blood flow, thinning of the myometrium overlying the placenta, loss of retroplacental “clear space”, protrusion of placenta into the bladder and increased vascularity of the uterine serosa – bladder interface. Vaginal sonography enables a more precise assessment of cervical infiltration. The following procedures are possible:

1. Caesarean hysterectomy, particularly in the case of severe bleeding from the placental site (e.g., following “iatrogenic” separation of the placenta).
2. Delivery of the infant without touching the placenta (e.g. transverse incision of the fundus in the case of deep anterior wall placenta percreta) and keeping the placenta in utero.
3. If the intraoperative diagnosis is confirmed, hysterectomy can be performed following delivery of the baby without trying to detach the placenta.
4. Focal resection of the affected uterine wall and preservation of the uterus.
5. Focal intracavitary Z-sutures to achieve haemostasis in small areas.

The antenatal diagnosis including the myometrial extent of deep placental invasion is essential for the appropriate operative planning. Following the above option (2), an expectant management for several weeks is possible if the placenta is left in situ after CS or even after spontaneous delivery (in non-praelevia). These patients should be closely followed up to ensure complete resolution, delayed spontaneous delivery or removal of the placental mass (with or without curettage). Currently no consensus exists about complementary treatment in conservatively treated patients. This approach potentially reduces the hysterectomy rate, bleeding and bladder lesions, but exposes the woman to additional (infectious) risks.
Hypogastric artery ligation for intractable pelvic hemorrhage

Zoltán Papp

Budapest, Hungary

Life-threatening peri-partum uterine bleeding remains a serious concern in obstetrics and gynecology, as it is a common cause of pregnancy-associated maternal mortality and severe morbidity. At present, post-partum hemorrhage (PPH) is one of the five leading causes of maternal mortality worldwide. Massive hemorrhage after child-birth occurs with a frequency of 1 or 2 in 1000 deliveries in the industrialized countries, and it is even more prevalent in the developing world. Beside surgical injury of the lower female genital tract or the uterus, clinical entities of PPH include uterine atony and abruption placentae, placenta praevia, increta, and percreta. In many cases, PPH can effectively be treated pharmacologically with intravenous infusion of either oxytocin or prostaglandins for uterine atony. In a subset of parturients, however, primary post-partum bleeding might remain refractory to aggressive medical treatment.

Historically, the only available treatment for these resistant cases was post-partum hysterectomy with loss of future reproductive potential. At present, a spectrum of operative means spanning from ligation of the uterine arteries, stepwise devascularisation of the blood supply to the uterus, or recently introduced uterine brace (B-Lynch) suture to ligation of the hypogastric (internal iliac) arteries exist for the control of intractable post-partum bleeding. Moreover, in recent years, arterial embolization has become a reliable non-surgical alternative to post-partum hysterectomy.

At present ligation of the hypogastric arteries is one in a spectrum of operative methods to control life-threatening post-partum hemorrhage before hysterectomy. Bilateral ligation of the internal iliac artery does not result in complete blockage of but a significant decrease in the blood supply of the female pelvic organs. Soon after ligation three previously existent collateral circulations will develop. Due to the smaller caliber of these arteries, the arterial pulse and pulse pressure are virtually eliminated. The effectiveness of this procedure in avoiding hysterectomy for post-partum hemorrhage has been reported in up to 50% cases. It has no adverse effect on subsequent fertility or pregnancy outcome, however, serial control for intrauterine growth restriction of the fetus is recommended.

Ligation of the hypogastric arteries is a safe surgical method, in at least a subset of women, to control excessive obstetric bleeding in those refractory to pharmacologic treatment. In obstetric emergencies caused by excessive bleeding, hypogastric artery ligation should be considered to be performed as a first step during laparotomy. The primary goal of the procedure is not to preserve the uterus but to control bleeding that, in a significant per cent of cases, might be enough to overcome the emergency situation. If the procedure alone or in combination with other methods are unable to control bleeding, hysterectomy is inevitable. It is emphasized that the biggest pitfall with hypogastric artery ligation is waiting too long to perform it. The procedure should be taught during obstetric and gynecologic training.
Uterine compression suture techniques and nontraditional surgical techniques

Philipp Steer

London, UK

Uterine atony causing postpartum haemorrhage following childbirth has for more than a hundred years being treated primarily with oxytocics. When they failed, surgery was directed at interrupting specific blood vessels (for example, ligation of the uterine artery or the internal iliac artery), and if that failed, the last resort was hysterectomy. In 1997, Lynch and colleagues published the revolutionary concept of the uterine compression suture, in which effectively the whole uterus was ligated. Initially only five cases were reported, but once the concept had been published, other surgical methods of compressing the uterus were developed, including square suturing, simplified approaches such as the Hayman suture, and other techniques to be used in less common circumstances (such as bleeding from the lower segment following removal of placenta accreta). Although there have been no randomized trials, multiple case series attest to success rates of 90% or more. Perhaps inevitably, complications have now been reported, the most important of which relate to uterine necrosis resulting from excessive prolonged interference with blood flow to the uterus. Other complications include intrauterine adhesions. However there are now many reports of successful subsequent pregnancies, suggesting that the complication rate is relatively low. Particular care needs to be taken if the technique is supplemented by the use of intrauterine tamponade with balloons.
Conservative in accreta: One-step conservative surgery

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Due to the increase of caesarean surgeries around the world, as well as the rise in complications that these imply, the one-step conservative surgery appears as alternative to solve the placental invasion and uterine tissue reconstruction in one surgical act. The design of this technique was possible after deep and continuous anatomic research, especially to understand certain circulatory phenomena following hemostatic measures. This vascular behavior called attention, as there is no correspondence among surgical practice, literature or in scientific articles. Therefore, after ten years of anatomy study, a new anastomotic component of the uterus could be established. This system explains, among other issues, how the uterus maintains its vitality after occlusion of the uterine arteries, and even after the joint occlusion of both uterine arteries and of the superior ovarian anastomotic pedicle. This anatomical knowledge was essential to perform an accurate hemostasis and fascial dissection in relation with placental invaded areas. Although this surgery is complex, it efficiently solves the problem in one surgical step. Surgery can usually be performed through a Pfannenstiel incision, and it usually takes between 50 and 90 min. This approach requires advanced surgical training and management of proximal vascular control, pelvic dissection, bladder detachment and uterine hemostatic methods. After more than 350 procedures, the one-step surgery has proved to be safe and inexpensive. Until this moment 52 pregnancies had been registered after this reconstructive surgery, no one had accreta recurrence, postpartum hemorrhage or other complications.
Postpartum hemorrhage: Use of fluids and blood products

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Postpartum hemorrhage (PPH) remains one of the top causes of preventable maternal mortality worldwide. Along with medical and surgical therapies, blood component therapy (BCT) is an integral component of PPH management. In many centers, current BCT strategies are based upon Advanced Trauma Life Support (ATLS) guidelines, which start resuscitation with crystalloid solutions followed by packed red blood cells (PRBC), while administration of other blood products such as fresh frozen plasma (FFP) and platelets (PLT) is based upon laboratory Results. Uterine blood flow at term may exceed 500mL/minute. Thus exsanguination may occur rapidly during severe PPH, leaving no time to wait for laboratory tests and rendering further BCT empirical. In the trauma literature, massive transfusion (MT) is often defined as administration of >10 units of PRBC within 24 hours. MT protocols at many US trauma centers do not recommend administration of FFP until after 4-10 units of PRBC have been given and many do not include specific recommendations for PLT transfusion until laboratory assessment documents thrombocytopenia. Recent retrospective studies published in the non-obstetric (trauma) literature, initially from military experience (Afghanistan and Iraq) and more recently from civilian experience (Level 1 trauma centers) have shown improved outcomes (most notably, significantly reduced mortality rates) with higher (i.e. 1:1) ratios of FFP: PRBC and PLT: PRBC administered early during MT. The purpose of this presentation is to review the recent evolution of MT in trauma and how this information may be applicable in the obstetrical arena to cases of severe PPH.
Obesity and pregnancy: Maternity under the XXI century pandemic, a GLOBE warning

Juan Carlos Bello Munoz

Obesity’s prevalence has grown among developed and developing countries. Because of a number of factors that have changed the nutritional profile for 80% of people in the planet, and the increasing use of cheap food – fast food, the percentage of obese women in fertile age has changed in America and part of Europe from 10 to 12% in the eighties to 25 to 30% in 2006. According to WHO classification for Body Mass Index, near 50% of world’s population has overweight, while nearby 23% is obese, approximately 20% of them, morbidly obese, which means ill because of obesity. Taking these numbers to public health matters one can easily conclude that, first, obesity has grown more and quicker than any other epidemic disease in history, and second the costs in terms of secondary attention and medical care of complications related to obesity is expressed in billions of Euros, just in Europe.

Maternity is, perhaps, the more sensitive state for weight changes in women’s life. Therefore weight changes in previously overweight or obese women can be particularly severe. According to literature, the fact of commencing a pregnancy with only overweight doubles the risk for adverse pregnancy outcome, particularly gestational diabetes, gestational hypertension and severe preeclampsia. Also doubles risks to the fetus for presenting macrosomy, mechanical distocia and intrapartum fetal distress. And increases significatively the risk for caesarean section, operative vaginal delivery, postpartum haemorrhage, some fetal cardiac and abdominal anomalies and stillbirth. It is also remarkable that 40% of maternal deaths in the world occurred to obese women.

Furthermore, all the abovementioned risks rise exponentially as the BMI increases, arriving to risks as high as 34 times for stillbirth in severely obese women with intrauterine growth restriction. Just for giving more complexity to the picture, those risks are not the same for all women, but vary widely according to ethnic origin, social and geographical conditions. The real impact of these additional factors upon the baseline risk for adverse pregnancy outcome remains unknown. And its relevance, considering the uprising of this pandemic condition is becoming crucial. That is why a multi country observational study evaluating the relationship amongst all those potentially confounding factors and obesity, in the quest for a customized risk for the obese pregnant patient is about to start.
Weight management programmes for overweight new mothers

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Background: Obesity now presents a major global health challenge. Within the UK, health fears about obesity are widespread. Scotland is reported to have the worst diet in Europe. Excess weight gain may occur during pregnancy; weight retention and increase are common postnatally. Postnatal weight loss is desirable for the woman’s own well-being; meeting parenting’s physical demands; minimizing obesity-related complications in future pregnancies; and promoting family health. Targeted postnatal weight-reduction interventions are desirable, but parameters must be defined before a definitive Randomized Controlled Trial can be devised.

Aims / Methods
This scoping study is using focus groups to explore recruitment, response and retention issues; identify group preferences for the intervention’s delivery, timing and setting; identify support for behavioral change; ascertain the motivators for initiating weight loss, and changes in diet and activity; identify relevant measures for both intervention and control participants in an RCT; and identify methods for assessing cost-benefits. Perceptions of realistic exercise, food and drink goals, modeling strategies and feedback opportunities are being explored.

Analysis: Analysis is gauging response to programs based on self efficacy and perceived behavioral control.

Summary of key findings: This study is underway. The author will present a discussion of the practical issues involved in accessing hard-to-reach populations; and preliminary findings concerning attitudes towards diet and physical activity among new mothers.

Conclusions and implications: The health benefits from minimizing obesity-related morbidity should be significant. Physical activity, dietary restriction and behavioral change are essential components of any changes in lifestyle in the obese population. We anticipate developing a portfolio of approaches, covering snacks/meals/drinks, physical activities, and approaches to goal setting.
Dietary intervention programme for mothers with raised BMI in early pregnancy

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The rise in obesity in the general population is reflected in the proportion of women obese in early pregnancy more than doubling in the past decade. Obesity in pregnancy is associated with increased risk of multiple complications which together with excessive maternal weight gain during pregnancy means obesity is now considered the most common clinical risk factor in obstetric practice. This has considerable implications for both the mother and her family, and the maternity services. While studies in non-pregnant obese women suggest that even a moderate weight reduction may have significant health benefits, women are advised not to try to lose weight during pregnancy. As part of the development of a dietary intervention program aimed at optimizing maternal weight gain during pregnancy for obese women, several issues have been identified in the preliminary stages which need to be considered when developing an intervention for this target group. Our data has shown a reluctance of obese mothers to address the issue of their weight in pregnancy. Furthermore Midwives are reluctant to raise the issue of obesity, despite an awareness of the associated risks for Mother and baby. Midwives themselves have little awareness of the service-use impact of obesity in pregnancy in terms of screening difficulties, the physical impact on Sonographers and on NHS financial resources. They see addressing the issue of obesity and pregnancy as a specialist area, out with their current knowledge base. They agreed the potential of specific targeted information for this group of mothers, and identified the need for support and training if they were required to deliver it. These findings suggest that we may need to initially focus on identifying and supporting the educational needs of Midwives, to enable them to effectively address the issue of obesity in pregnancy with the women in their care.
The etiology and prevention of congenital malformations

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Physicians play a major role in diagnosing and treating children with congenital malformations before and after they are born. Clinicians should realize that there have been amazing advances in teratology in the last 50 years. We still cannot provide the families with a definitive diagnosis for every child. However, a multitude of genetic causes and environmental teratogens (agents that produce congenital malformations from exposures during pregnancy) have been discovered. It is important to remember that environmentally produced birth defects are potentially preventable. There are a number of important clinical teratology rules that are useful to clinicians.

1. No teratogenic agent should be described qualitatively as a teratogen, without describing the dose and the time in pregnancy when the embryo is at risk.
2. Even agents that have been demonstrated to Result in malformations cannot produce every type of malformation. It is easier to exclude an agent as a cause of birth defects than to definitively conclude that it was responsible for birth defects.
3. Teratogenic agents follow a toxicological dose-response curve. This means that each teratogen has a threshold dose, below which, there is no risk.
4. The evaluation of a child with congenital malformations cannot be adequately performed unless it is approached with the same scholarship as the evaluation of any other complicated medical problem.
5. Following an in utero diagnosis of a congenital malformation the physician informs the parents about their options in an accurate and compassionate manner. It is the parents that decide which options will be selected.
Currently, around the world, there are a multitude of glucose challenges and threshold criteria for the diagnosis of gestational diabetes. Some, such as the O'Sullivan criteria, were based upon the statistical assessment of two standard deviations above the mean in a population of pregnant women, and were validated by their predictive values for subsequent diabetes in the mother. Others, such as the World Health Organization criteria, were based on values for non-pregnant adults. None were based upon their ability to identify pregnancies at increased risk for potentially preventable adverse perinatal outcomes. In 1991, the Third International Workshop Conference on Gestational Diabetes met in Chicago. Noting the above state of confusion and the resultant inability to compare providences among different populations, the group recommended that the 75 gram challenge be universally employed. In 1998, the 4th IWC on GDM concluded that “...there remains a compelling need to develop diagnostic criteria...based on the specific relationships between hyperglycemia and the risk of adverse outcome.” The HAPO (Hyperglycemia and Adverse Pregnancy Outcome) Study was designed to determine what level of glucose intolerance during pregnancy, short of diabetes, is associated with the increased risk of adverse outcome. Approximately 23,000 women in 15 centers in 9 different countries underwent a blinded 75 gram, 2-hr OGTT at 24-32 weeks gestation (mean 28 weeks). There was a continuous relationship between each of the three glucose values and each of the primary outcome variables: birth-weight >90th %ile, caesarean section delivery, clinical neonatal hypoglycemia, and cord blood C-peptide >90th %ile. The relationship held even when corrected for race, ethnicity, country, BMI and a number of other potential confounders. An international group of interested individuals and organizations is currently working to build consensus around a set of diagnostic criteria that are based upon pregnancy outcome. The process being utilized and the relationship between glucose and some of the secondary outcome variables will be described in this presentation.
Effect of timing of first postnatal care home visit on neonatal mortality in Bangladesh: An observational study

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Background: Postnatal home visitation by community health workers has been shown to be efficacious in reducing neonatal mortality, but the optimum timing of home visits remains undetermined. Using data from a community-based trial of neonatal care interventions conducted in Bangladesh during 2004-2005, we examined the effect of the timing of first postnatal home visit on neonatal mortality.

Methods: Community health workers were scheduled to visit newborns at home on days 1, 3, and 7 of life. Using data from community health workers’ visit records, time-varying discrete hazard models were used to estimate hazard ratios for neonatal mortality by the day of first postnatal visit, adjusting for confounding covariates. This method minimized survival bias.

Results: 9,211 live births were included. In the adjusted analysis, among those who survived the first day, a visit on day 1 was associated with 67% lower neonatal mortality (hazard ratio: 0.33; 95% confidence interval: 0.23 to 0.46) compared to those who received no visit. For those who survived the first two days of life, receiving the first visit on the second day was associated with a 64% lower neonatal mortality (hazard ratio: 0.36; 95% confidence interval: 0.23 to 0.55). First visits after the second day of life were not associated with reduced mortality.

Conclusions: In developing country settings, especially where home delivery with unskilled attendants is common, postnatal home visits within the first two days of life by trained community health workers can significantly reduce neonatal mortality.

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Predictive factors for intrauterine growth restriction in women affected by pregnancy-related hypertensive disorders compared with healthy women

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Objective: While pregnancy-related hypertensive disorders (PRHDs) seem to origin by placental vascular anomalies, intrauterine growth restriction (IUGR) may be the Result of a fetal perfusion imbalance. Our study investigates the predisposing factors for IUGR in women with PRHDs.

Methods: We selected 350 women with PRHDs between 2004 and 2008, and a random control cohort without pregnancy complications. We asked them and their partners about personal and clinical information, and familiarity for some common pathologies. Statistical analysis was performed by R considering significant p<0.05. Also multivariate analysis was performed.

Results: Among 441 contacted women, 210 have a diagnosis of PRHDs and 44 of them also of IUGR. Among women affected by PRHDs, IUGR Results influenced by maternal grandmother trombophilia (p<0.05) and epilepsy (p<0.05), maternal grandfather hypertension (p0.090) and trombophilia (p0.053). If compared with the healthy obstetric controls, IUGR correlates (p<0.05) also with maternal chronic hypertension and diabetes and paternal trombophilia, fibres-poor diet, low educational level, multiparity, multiple pregnancy and stress during pregnancy, requiring in the most cases caesarean section. By multivariatre analysis, IUGR in women affected by PRHDs seems influenced by maternal grandmother trombophilia and grandfather hypertension (p<0.05), while maternal age and chronic hypertension (p0.056) Result protective. If compared with healthy obstetric population, IUGR risk increases by maternal grandmother trombophilia (p<0.05) and grandfather hypertension (p0.071), paternal trombophilia (p0.072).

Conclusions: Considering IUGR as a fetal circulation anomaly, its risk may depend on a combination of environmental and genetic factors, including familiarity for vascular and cardio-circulatory pathologies, such as hypertension and trombophilia.

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Introduction: Applying the phase-rectified signal averaging (PRSA) on ECG registrations is a method of detecting mortality after heart attacks in adult cardiology which is superior to other current methods. In a pilot study on fetal tracings we have derived a new parameter with PRSA - the averaged acceleration capacity (AAC). AAC is used for assessing dynamic capacity which reflects especially the sympathetic part of the fetal autonomic nervous system. This method enables us to better distinguish between average and growth restricted fetuses than the current short term variation (STV) of Dawes/Redman.

Materials and methods: We present the Results of a prospective analysis: 39 patients with growth restricted fetuses (<10. percentile) and a resistance index of the A. umb. >95. percentile were matched with 43 women belonging to a control group with normal pregnancies. All women underwent Doppler-examinations as well as cardiotocograms. The latter were analyzed by the Oxford Sonicaid 8002 system for STV and by applying the PRSA for AAC. Both Results were compared regarding the prediction of fetal compromise.

Results: AAC produced better Results than STV for distinguishing between growth retarded and average fetuses.

Conclusion: AAC is a complex and fascinating parameter providing additional information on fetuses with growth restriction. Up to now, AAC is only available by offline analysis. Thus, technical progress is essential for direct application of PRSA on CTG or ECG. Furthermore, longitudinal studies are necessary to assess AAC during development of pathologic Doppler flow patterns.
Placental pathologies in fetal MRI – can we predict the impact on perinatal outcome?

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Introduction: Placental pathologies represent a risk for insufficient supply of oxygen and nutrients to the fetus. Intrauterine growth retardation (IUGR), prematurity, and intrauterine death can be a consequence. The purpose of this study was to evaluate whether currently available MRI techniques can predict the impact of placental pathologies on the perinatal outcome.

Material and Methods: In a retrospective study 223 patients between gestational weeks 17 and 37 with placental pathologies on MRI scans were investigated on a 1.5 Tesla MR. Placental pathologies were described in etiology and size. Prematurity, IUGR, mortality, as well as severe cerebral morbidities were evaluated.

Results: 116 placentas showed placental infarctions, 39 subchorionic thrombi, 12 intervillous hemorrhage, 7 retroplacental hematomas. 118 showed pathologic placental maturation. Prematurity rates were 81% (n=182), IUGR was 42% (n=95), perinatal mortality rates were 26% (intrauterine n=42, neonatal n=18). Of the 163 surviving patients 9% had severe cerebral morbidities (5 IVH III-IV, 11 PVL II-IV).

Discussion: Magnetic resonance imaging is a useful tool in the investigation of placental pathologies. High rates of prematurity, growth retardation and mortality underlines the importance of correct interpretation of placental pathologies, to improve perinatal management. The extent of the pathology in relation to placental volume should be further analyzed.

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Management and outcome of fetal supraventricular tachycardias –
a single institution’s experience

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Objective: To evaluate the efficacy of prenatal antiarrhythmic therapy of supraventricular tachycardia (SVT) and atrial flutter (aF) during fetal life as well as the pre- and postnatal outcome.

Methods/Results: SVT was diagnosed in 23 consecutive fetuses, 20 with SVT and three with aF. Diagnosis of the arrhythmia was made at a mean of 32 weeks of gestation. Fetal ventricular heart rate ranged from 170-305bpm. Signs of heart failure were present in 13 (57%). Medical treatment was started with maternal iv or oral digoxin in all but two cases. This resulted in a sinus rhythm in 12 (57%) after a mean of 7 days. A second drug (verapamil 2, flecainide 7) was added in 9 fetuses which restored a sinus rhythm in all after a mean of 15 days.

After birth treatment was stopped in all but 4 newborns. Eleven patients (48%) remained free of tachycardia during a follow up of 1-21yrs. Twelve patients (52%) suffered a recurrence of SVT: one remained without therapy, six became tachycardia free after one year of treatment, five needed further medication beyond the age of one year. Postnatal classification of the tachycardia from surface ecg was: atrioventricular reentry tachycardia (6), permanent junctional reentry tachycardia (2), focal atrial tachycardia (3), multifocal atrial tachycardia (1).

Conclusion: Sinus rhythm was achieved in 100% of the prenatally treated pts and was maintained postnataally in 48% without any therapy. Altogether SVT ceased in 78% after the first year of life. A consistent pharmacologic treatment is needed to control prenatal SVT.

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After combined screening for chromosomal abnormalities, how can mother’s age influence the decision towards invasive procedures?

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Every woman has an age-related risk of having a fetus with chromosomal abnormality. First trimester screening for trisomy 21 is actually based on fmf criteria. Low risk screening, may reassure pregnant women and make them avoid invasive technique. High risk screening can undergoes to invasive procedures that has 1% risk of miscarriage. If well counseled, women doubt about invasive testing. During 2008, 1296 pregnant women, went on FMF first trimester screening for Down syndrome in our Clinic. High risk test was when 1/300. Mean age was 32.7 years and 37% were over 35 yso. Of this group, 92% had a decrease in age-related risk after screening test (negative): 71% choose not to have CVS and 29% underwent to it. Of the 38 women over 35 yso and a positive screening, 82% choose CVS while 18% did not had anything. Among the 816 women under 35 yso, 99% had a negative screening, of which only 16% choose CVS. 97%of positive screening into under 35 yso group went on invasive procedures.

Conclusions: Our data shows that young women, aged under 35 years old, keep on spin off decision: If screening test is negative, approximately 95% do not go to invasive procedure, while, if the test is positive, about 100% go to invasive technique. Older women, show: In fact when test is positive, although the age, only about 80% go to invasive test and if it is negative, about 70% decide not to have any risk of miscarriage undergoing to invasive test.

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Diagnosis, Treatment and Prognosis of Fetal Tumors

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Introduction: Fetal tumors (FT) are uncommon, benign or malignant masses, diagnosed in uterus, which may cause serious illness in the fetus or the newborn, with a variable prognosis. Fetal ultrasound plays an important role in the diagnosis and follow-up of FT.

Objective: Characterize the fetal and newborn population with the diagnosis of FT sent to our prenatal diagnosis consultation in terms of: gestational age at diagnosis, type/location of the tumor and postnatal diagnosis concordance.

Methods: Prospective evaluation of the fetuses with the diagnosis of fetal tumor during January 2003-December 2006.

Results: 14 fetal tumors were diagnosed, with a mean age of diagnosis at 23 weeks. 7/14 were located in the abdominopelvic region, 3/14 in the sacrococcygeal region, 3/14 in the thoracic region and 1/14 in the cervical region. Fetal magnetic resonance was performed in 7/14 fetus. There was one case of polyhydramnios, which turned out to be the only case of medical interruption of pregnancy. Eight tumors were confirmed in the neonatal period: 2/8 sacrococcygeal teratomas, 1/8 neuroblastoma, 1/8 simple hepatic cyst, 1/8 mixoma of the tricuspid valve, 1/8 ovarian cyst, 1/8 cystic lymphangioma, 1/8 broncogenic cysts.

Of the 8 tumors confirmed in the neonatal period, 5 were treated surgically.

Of the 5 cases not confirmed in the neonatal period, 4 had no pathology at follow-up and one case had a different diagnosis.

Comments: Sacrococcygeal teratomas were the most frequent tumor in our study. Although the prognosis of fetal tumors is generally poor, in our population the prognosis was favorable in all cases.

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Oncostatin M as a target biological molecule of preeclampsia

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Object: Given the presence of the cytokinetic effects of Oncostatin M (OSM), we hypothesized that placental expression of OSM and serum OSM levels are elevated in preeclampsia. To verify this hypothesis, we determined the expression of OSM in placenta and levels of OSM in plasma form women with preeclampsia and normal pregnant women.

Methods: Sixteen women with severe preeclampsia and sixteen normal pregnancy women were studied. Placental tissues were immediately frozen and stored at -80°C until extraction of total RNA. Total RNA was extracted and real-time quantitative PCR was carried out. Placental tissues fixed in 4% paraformaldehyde were reacted with antibodies against OSM. An pathologist reviewed these stained slides. The maternal serum and umbilical venous concentration of OSM were determined by ELISA analysis.

Results: The mRNA expression level of OSM in preeclamptic placenta was increased by 3.91 times which was significantly higher than those of the normal group (P=0.028). OSM immunoreactivity was significantly higher in placentas of patients with preeclampsia than placentas from the normal group. The significantly greater OSM expressions were noted in cytotrophoblasts, syncytotrophoblasts and endothelium of preeclamptic placentas as compared to normal placentas (respectively, P=0.004, 0.001 and 0.04). OSM concentration of preeclamptic women’s serum was significantly higher than that of normal women’s plasma (P=0.016). However, OSM level of umbilical venous serum was not significantly different between two groups (P=0.243)

Conclusion: OSM may play a biological marker for severe preeclampsia, and its action may be predominantly on the trophoblasts and endothelium of placenta villi in preeclampsia.

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Can we predict GDM onset with nuchal translucency measurement in the first trimester?

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Background and aims: This study was planned to evaluate whether increased Nuchal Translucency (NT) thickness in the first trimester of gestation can be related to onset of Gestational Diabetes Mellitus (GDM) during pregnancy.

Methods: From January 2006 to August 2008, a group of 678 singleton pregnancies who had developed GDM has been selected among a total of 3966 pregnant women who had undergone first trimester screening for aneuploidies at 11-13 weeks of gestation. The ones whose NT thickness was above the 95th centile (n=9) were excluded from the study and the other 669, with NT under the 95th centile, were selected as the study group. A group of 420 single pregnant women with physiological pregnancy and NT under the 95th centile were enrolled as control group.

Both fetal and cariotype’s anomalies were excluded in the two groups.

NT was measured by a Fetal Medicine Foundation certificated operator; GDM was diagnosed at 24-28 weeks of gestation following Carpenter and Coustan criteria.

In the analyzes of continuous variables, study and control group were compared by Student’s t-test and Anova test.

Results: There was no significative difference (p=0.585) between NT values in the study (mean=1.56) and control group (mean=1.54).

Conclusions: Nuchal Translucency thickness does not show a significative increase in those women who subsequently develop Gestational Diabetes Mellitus. Therefore, GDM onset cannot be predicted using an ultrasound parameter as NT assessment.

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Free communication 2: Nutrition and metabolism in mother and infant/
Metabolic disorders in the newborn

High salt intake and oxidative stress in the kidney – the role of fetal programming

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High salt intake causes hypertension and adverse cardiovascular and renal outcomes, but some forms of salt-mediated target organ damage are blood pressure-independent. It has been suggested that high salt intake during pregnancy influences blood pressure in the offspring. It was the purpose of the present study to clarify whether high salt intake in pregnancy and after weaning alters blood pressure and kidney morphology in the offspring. Sprague-Dawley rats were fed normal (0.15%), medium (1.3%), or high (8.0%) salt diet during pregnancy and weaning. The offspring were weaned at 4 weeks of age and subsequently maintained on the same diet or switched to normal or high salt diet respectively. Kidney morphology and markers of oxidative stress were assessed at 7 and 12 weeks postnatally. The number of glomeruli in the offspring of the mothers on high salt was significantly lower compared to the other groups. Compared to other offspring urinary 8-isoprostane was significantly higher in offspring of mothers on high salt irrespective of their post-weaning salt intake (8.6±3.1 and 2.5±0.6 vs. 0.8±0.5 and 1.1±0.4mg/24h). Albumin excretion was higher (5.8±5.5 vs. 0.5±0.3mg/24h) and creatinine clearance (1.5±0.4 vs. 2.5±1.1ml/min) was lower in offspring of mothers on high salt which were maintained on high salt compared with other offspring. No significant differences in telemetrically measured blood pressure were observed between the groups of offspring. High salt intake in mothers restricts nephron number in offspring and predisposes the offspring to increased oxidative stress and disturbed kidney function.

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The effect of ω-3 long-chain polyunsaturated fatty acid (LCPUFA) supplementation during pregnancy on infant adipose tissue development

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There is some evidence that the composition of fatty acids, particularly the ratio of ω-6/ω-3 LCPUFAs in the maternal diet during pregnancy may play a role in adipogenesis during the fetal and early postnatal period and thus affects the risk of developing obesity in early life. Therefore the INFAT study - a prospective, randomized, controlled intervention trial – was initiated to examine whether a decrease in the ratio of ω-6/ω-3 LC-PUFA intake is associated with less expansive adipose tissue growth in newborns.

From gestation week 15 until delivery, 112 pregnant women were either supplemented with 1.05g docosahexaenoic acid (DHA) and 0.18g eicosapentaenoic acid (EPA) and simultaneously reduced their arachidonic acid (AA) intake to 0.1g/d (intervention group) or followed their habitual diet (control group). Adipose tissue mass of the newborn was assessed by skinfold thickness measurement. Data on maternal and cord blood LC-PUFAs, pregnancy outcome and infant anthropometry were also collected.

Compared to the control group, the intervention group showed significantly increased maternal and cord DHA and EPA (% by wt) and reduced maternal AA (P ≤0.001) in plasma and red blood cells. Pregnancy outcomes and infant growth parameters did not differ significantly between the two groups.

Our preliminary data suggest that a reduced ratio of ω-6/ω-3 LC-PUFAs in the maternal diet during pregnancy is followed by a significantly reduced ω-6/ω-3 ratio in maternal and cord blood. A careful long-term follow up of infant anthropometry is currently performed.

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Nutritional problems and management of lean pregnant women

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Objective: The average birth weights in Japanese neonates are decreasing. This report highlights the effects of lean pregnant women on obstetric and perinatal outcome.

Study Design: An analysis was performed of all Japanese deliveries at Nihon University Itabashi Hospital. In this population-based retrospective cohort study, the perinatal data of pregnant women was divided into three groups. The lean women in their non-pregnant periods were compared to data of normal women. Univariate analysis was used to assess the effect of BMI on pregnancy outcomes. Observed complications during the pregnancy and delivery were also calculated.

Results: The rate of lean pregnant women among all Japanese women was 10.7%. BMI of the lean pregnant women in their non-pregnant periods were 17.2±0.8, and BMI of the normal pregnant women in their non-pregnant periods were 20.5±1.5. The lean pregnant women were taller than the normal women, and the former were lighter than the latter. The weight gains in the lean pregnant women were bigger than those in the average pregnant women.

The lean pregnant women were found to have significantly higher rates of obstetric complications such as threatened abortion, threatened preterm delivery and urinary tract infections. Perinatal morbidities and mortalities of fetuses were increased in lean pregnant women with IUGR, IUFD and oligohydramnios.

Conclusion: I think that being skinny during the reproductive period has important effects upon an incidence of SGA babies and it is necessary for lean pregnant women to attain adequate weight gains.

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Amniotic fluid iodine concentration in growth restricted versus normal fetuses


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Introduction: Newborns with growth restriction might be related to iodine deficiency during pregnancy through a thyroid function alteration. This status of iodine deficiency could be demonstrated by low iodine concentrations in amniotic fluid.

Methods: In 34 Pregnant women delivered at Virgen de las Nieves University Hospital, Granada (Spain), 21 cases with intrauterine growth restriction and 13 controls normal growth fetuses matched by gestational age, maternal and fetal blood samples at the time of delivery were collected to determine TSH, and maternal urine and amniotic fluid to determine iodine concentrations.

Results: Mothers with growth restricted fetuses showed higher urine iodine concentrations than that with normal fetuses (110.1 vs. 73.45 µg/l) (p<0.05). No difference in iodine concentrations in amniotic fluid were found in both groups. Growth restricted fetuses showed also a high incidence of hypothyroidism but not significantly higher levels of TSH than normal fetuses (9.41 vs. 5.94µUI/ml). No difference was found in maternal blood TSH concentrations in both groups.

Conclusion: Growth restricted fetuses show a high incidence of hypothiroidism at birth, but there are no differences in iodine concentrations in maternal urine or amniotic fluid regarding normal growth fetuses.

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Hypoglycaemia induces oxidative stress in small for gestational age term newborns

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Introduction: Recent data suggest that peroxynitrite generation and subsequent protein nitration occurs in the neonatal brain after hypoglycaemia in animal models. Our previous studies demonstrated that plasma albumin nitration increased during hypoglycaemia in preterm infants. In this study, we investigated albumin nitration after hypoglycaemia in term newborns.

Material and methods: Using a novel ELISA, we measured nitroalbumin concentrations in venous plasma taken at 1-4 (D0) and 18-24 (D1) hours of life from 29 SGA term newborns without any other obvious cause of nitrative stress. During the first 48 hours of life, glycaemia was monitored every 3-4 hours by a strip method. We investigated the significance of differences in nitroalbumin concentrations with regard to the occurrence and recurrence of hypoglycaemic episodes (EHG: glycaemia <2.5mmol/l).

Results: D0 and D1 nitroalbumin concentrations were significantly higher in patients who developed at least 1 EHG than in normoglycaemic patients. Among hypoglycaemic SGA, D1 nitroalbumin concentration was higher in infants who developed >2 EHG than in infants with only 1 or 2 episodes. We also observed significant correlations between D1 nitroalbumin concentration and first glycaemia (r=0.67, p<0.05), glycaemia during the first 18 hours of life (r=-0.87, p<0.001) and the delay between the last EHG and the D1 plasma sample (r=-0.90, p<0.001).

Conclusion: Recurrent episodes of hypoglycaemia during the first 24 hours of life are associated with increased albumin nitration in SGA term newborns. This indicates the occurrence of nitrative stress implying a risk of end-organ damage due to protein nitration and lipid peroxidation.

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Fecal calprotectin and mode of feeding in young infants

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Objective: The protein calprotectin, released by neutrophils, has regulatory actions on the immune system. Fecal calprotectin levels are currently used as a marker of activity in inflammatory bowel diseases. In neonatal age, fecal concentrations of calprotectin are extremely high, compared to adults. We determined fecal concentration of calprotectin in healthy, infants at 3 months of age, to verify whether the mode of feeding has effects on these levels.

Patients and methods: We enrolled 59 healthy term (gestational age >37 weeks) at a postnatal age of 12 weeks (range: 10-15 weeks), exclusively breastfed (HU group) or with a starting formula (FM group). Fecal calprotectin was measured by an immunoenzyme assay (Calprest®, Eurospital, Trieste, Italy) on a single sample of stools.

Results: Mean concentration (+SD) of fecal calprotectin was 127+114ng/g in the HU group and 127+93ng/g in the FM group (p =NS). In both groups, we noted a trend, although non statistically significant, higher values of fecal calprotectin were shown by infants born by caesarean section, or with family history of allergies, or frequent regurgitation.

Conclusions: The finding of higher levels of calprotectin in young infants is in agreement with previous studies. The overlapping of the values of the two groups suggests that, in general, formula milk does not promote an activation of the intestinal immune system, compared to human milk. However, in infants with family history for allergic diseases, the slightly higher values of calprotectin may suggest a subclinical activation of the intestinal immune system.

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Comparation of leptin gestational levels in maternal serum and body fat composition in mothes with fetus IURG and mothers with normal fetuses

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Growth fetal retardation (IUGR) is one of the main perinatal patologies with great complications for the newborn and for future adult life. Causes of this patology are placental impairment and mother nutritional abnormalities. The main objective of our study is to determine the relationship between serum leptin levels in third trimester of pregnancy and the percentage of maternal body fat as an assessment of nutritional maternal status in cases of IURG and adequate weight for gestational age. This is a longitudinal and prospective case-control study of 127 pregnant women: 46 cases and 81 controls. A Dual Energy X-Ray Absortiometry (DEXA) is done in the first 14 days of postpartum.

Results: Value of leptin in cases is 17.57pg/ml and 14.662pg/ml for controls, being the difference in the limit of significance (p=0.066). We have not found significant differences in body fat distribution neither android nor ginoid in cases and controls. But there is a tendency to signification in de BMI (p=0.061). Discussion: DEXA can mesure mineral mass and body fat. Leptin is a peptide than regulates nutritional behavior and energetic balance. Serum levels of leptin are related with body fat mass and they mark the amount of fat mass in mothers. We have not found significant differences between both parameters but probably a major number of patients is required to achieve statistical differences for leptin.

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Treatment of IUGR human fetuses with chronic infusions of amino acid and glucose supplementation through a subcutaneously implanted intravascular perinatal port system

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Objective: Intrauterine growth restriction (IUGR) carries an increased risk of mortality and morbidity. The accepted procedure to treat IUGR fetuses is the delivery by caesarean section which may increase neonatal mortality and morbidity and deteriorates neonatal brain development.

Material and Methods
To develop a new treatment option for IUGR, intravascular catheters connected to a subcutaneous placed port system for systemic injection of drugs and fetal blood sampling were developed and successfully used in 24 fetal sheep. We report here on intravascular supplementation with amino acids and glucose of IUGR human fetuses at 33 weeks of gestation with oligohydramnios and brain sparing in Doppler using "Fetal nutrition port kit" (Norfolk Medical, Illinois, USA). The catheter was implanted into the umbilical vein (UV) by cordocentesis, and was then connected to subcutaneously implanted Port system. The treatment course included daily infusions of amino acid solution (VAMINOLACT, Pharmacia, Sweden) 25ml and 10% solution of glucose 25ml into UV.

Results: Daily intravascular fetal nutrition significantly improved Doppler parameters, brain sparing disappeared. No complications were seen. The patient was delivered by caesarean section in 38th week of gestation. The female newborn weighted 2,130g and was 47cm high. Blood sampling from UV after delivery showed no deviations of amino acids in comparison to standardized curves.

Conclusion: This is the first report of successful use of subcutaneously implanted intravascular perinatal port system in IUGR human fetuses for long term administration of nutriments into UV of fetus for treatment of IUGR and prolongation of pregnancy.

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The role of angiotensin II during fetal lung development: A possible molecular explanation for fetal lung hypoplasia induced by inhibitors of renin-angiotensin system

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Background: Maternal administration of angiotensin converting enzyme inhibitors (ACE-I) and angiotensin receptor-antagonists (ARA) can induce fetal lung hypoplasia. However, the role of renin-angiotensin system (RAS) on lung morphogenesis remains unknown. Our aim was to clarify the role of angiotensin II (AngII), endproduct of the RAS, during fetal lung development.

Methods: Fetal rat lungs were harvested at 13.5 days post-conception and cultured with increasing doses of AngII or selective antagonists of AngII type 1 (AT1R; ZD-7155) and type 2 (AT2R; PD-123319) receptors. Morphometric analysis was performed in all explants. STAT3, ERK1/2, JNK, p38 and PI3-AKT phosphorylation in lung explants treated with AngII, ZD-7155 and PD-123319 was assessed by Western blot.

Results: AngII supplementation induced a biphasic effect (lower doses increased, while higher doses had no additional effect) on lung growth. Selective activation of AT1R (using AT2R antagonist) and the lowest dose studied stimulated lung growth through ERK1/2 and JNK signalling pathway. Moreover, selective activation of AT2R (using AT1R antagonist) and the highest dose studied inhibited lung branching by decreasing p-38 and JNK phosphorylation and increasing STAT3 phosphorylation.

Conclusions: AngII in lower doses acts through AT1R and stimulates lung growth, whereas AngII in higher doses acts through AT2R and inhibits lung branching. These Results suggest that AngII, a classical endothelial mediator, is a new regulator of lung morphogenesis and propose that an airway-vasculature interaction can regulate fetal lung branching. Furthermore, these actions of AngII explain why ACE-I and ARA can induce fetal lung hypoplasia after maternal administration during pregnancy.

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Biobanking and networking – the way to successful scientific cooperation

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Biobanks are a collection of biological material (blood, DNA, tissue, biopsy specimens, etc) and the associated data and information stored in an organised system, for a population or a large subset of a population. By combining and comparing biological tissue samples with patient information, researchers will be able to investigate the fundamental mechanisms of diseases. So Biobanking offers new abilities for translating new biomedical knowledge into new clinical practices, diagnostic techniques and preventative treatments.

“Networker” is a colloquial expression for people who actively build up and enlarge a network. Networking is a “marketing” method by which research opportunities are created through networks of like-minded researchers. Due to specific research fields it is often necessary that Networking is conducted on a larger scale via the Internet in order to connect people from all over the world. In addition, being part of this network on specific platforms it is easier to find suitable sponsors. Networks now make globalization accessible also for small and medium sized companies. Biobanks form the base for networks in which enterprises and researchers cooperate. Networks have internationally established themselves as one of the most important instruments of the economic policy turned over.

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Acquired hypermethylation of the hypothalamic insulin receptor promoter in neonatally overfed rats

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Neonatal overnutrition leads to an increased risk of obesity and diabetes later in life. Rats overnourished neonatally by rearing in small litters develop permanent obesity disposition, which is accompanied by diabetogenic and cardiovascular alterations in terms of the metabolic syndrome. These animals show a neonatally “programmed” hypothalamic insulin resistance with permanent hyperphagia. Epigenomic mechanisms, like DNA methylation, might be responsible for processes of perinatal programming. We therefore investigated whether neonatal overnutrition leads to alterations of the DNA methylation pattern of the promoter of the insulin receptor gene. Neonatal overnutrition was induced by raising Wistar rats in small litters (3 pups per nest; SL) from day 3-21 of life. We investigated the hypothalamic DNA methylation pattern of a 615 bp fragment of the insulin receptor promoter, using bisulfite modification, cloning and sequencing. Although less than 1% of CpG dinucleotides of both groups were methylated, significant group differences were found within the 322 bp CpG island of the promoter. The proportion of animals which showed at least one methylated CpG was significantly increased in the SL group (p=0.04). Simultaneously, the percentage of methylated CpGs within the CpG island was higher in SL rats (p=0.01). For the first time, these data show that overnutrition during a critical developmental period can alter the DNA methylation pattern of a central nervous gene promoter. Alterations might predispose to decreased hypothalamic receptor expression and insulin sensing as causal factor for hyperphagia and perinatally programmed obesity disposition. Supported by the DFG (PL 241/4-1; GRK 1208)

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Developmental effects of cholesterol enriched hyperlipidic diets in rabbits

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The aim of this study was to determine the relative role of cholesterol and of the N3/N6 fatty acid ratio on fetal development using a doe model.

Twenty-five does were fed from 10 weeks of age with one of 5 diets: SC (Soy oil -9% lipids- + 0.1% cholesterol), S (Soy oil -8% lipids), RC (Rapeseed -8% lipids- + 0.1% cholesterol), R (Rapeseed -8% lipids) or Co (2% lipids, no cholesterol). Fetal growth was monitored. Pups were weighed at birth and the number of pups per lactating doe was equilibrated. All offspring were fed a control diet after weaning.

Although maternal lipid intake was significantly increased in all treated groups, does adjusted their intake and caloric intake and doe body weight were not statistically different between groups. Conceptus length was significantly reduced at D9 of pregnancy in SC (-14%) and RC (-5%) vs. C (p<0.05). At mid-term (D15), post-mortem analyzes did not show significant differences in fetal weight but placentas were significantly heavier in S compared to all other groups (P<0.05, N=11 to 33 conceptuses/group). On D28, a few days before term, fetal abdominal perimeter was significantly reduced in SC and RC groups (P<0.05). There was no significant difference in litter size. Birth weight was significantly decreased in all groups.

In conclusion, long-term cholesterol- and lipid-enriched diets induced intrauterine growth retardation in does with variable effects according to the n3/n6 fatty acid ratio and cholesterol dietary content, with more significant effects observed in the cholesterol-enriched diets.

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Mature and immature dendritic cells in intrauterine and extrauterine implantation

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Maternal dendritic cells (DC) are supposed to induce immunological tolerance to fetal trophoblast antigens in intrauterine implantation via NK cells and T cells. We examined different stages of DC in intrauterine and tubal pregnancies lacking NK cells to compare mechanisms of feto-maternal tolerance at both implantation sides.

Patients and methods: First trimester tissue specimens from elective abortions (IUP, n=10) and viable tubal pregnancies (VTP, n=7) were examined by immunohistochemistry for CD83 (maturated DC), DEC205 (activated but not fully maturated DC) and DC-SIGN (immature probably macrophage-like DC) alone and in doublestaining with CD14 (macrophages). Cytokeratin 7 was used to define the area of trophoblast invasion. Cell numbers were counted by two investigators independant from each other in 5 defined areas and analyzed using the two-tailed t-test (p<0.05).

Results: There was a gradient from a large number of immature DC-SIGN+ DC (57.5 cells/mm² in IUP and 47.4 cells/mm² in VTP, p=0.49) over an intermediate number of activated but not fully maturated DEC205+ DC (2.28 and 2.96 cells/mm², p=0.66) to a low number of mature CD83+ DC (0.83 and 0.44 cells/mm², p=0.1). More than 2/3 of DC-SIGN+ cells (67% and 85%) were also CD14+.

Conclusion: The almost equal distribution of CD83+, DEC205+ and mostly macrophage-like DC-SIGN+ cells in IUP and VTP suggests a significant role of mature and immature DC for the development of feto-maternal tolerance in intrauterine and extrauterine pregnancy. This Result points at a comparable immunological process of intrauterine and extrauterine implantation dependant on the interaction partners available.

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Acute hypoxia decreases system: A amino acid transporter activity in placental villous explants

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Human fetal development is dependent upon an adequate supply of amino acids from the maternal circulation. Fetal growth restriction is associated with lower fetal amino acid concentrations and lower placental amino acid transport. One mechanism by which placental amino acid transport may be adversely affected is villous hypoxia as a Result of placental underperfusion.

Objective: To test whether acute hypoxic conditions influence system A amino acid transporter activity in placental villous explants.

Methods: The uptake of C14-methyl-aminoisobuteric acid (MeAIB) (n=3) was determined after incubation of a triplicate set of primary villous fragments isolated from placentas of primiparous women with uncomplicated pregnancies for 10, 30 and 120 minutes under hypoxic (2% oxygen) and standard (20% oxygen) conditions. Data are presented as mean ± SEM. Statistical analyzes were performed with a paired t-test, probability values were considered significant at p<0.05.

Results: Hypoxia significantly decreased system A amino acid transport activity in placental villous fragments by 60%, 72% and 90% after 10, 30 and 120 minutes, respectively (p=0.029, 0.005, 0.0016) compared to standard conditions. The decrease in system A activity was significant within 10 minutes of hypoxia exposure (7.76±0.46 vs. 19.64±0.44 pmol/mg/40min, p=0.029).

Conclusions: Our data suggest that hypoxia has a remarkably acute effect on placental amino acid transport. Several mechanisms may account for this robust acute effect including changes in transcription, translation or post-translational changes of System A transporter proteins.

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Do human amniotic fluid stem cells differentiate into neurons in vitro?

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It has been shown that amniotic fluid stem cells (AFSCs) have a great differentiative potential. In order to evaluate whether AFSCs are able to differentiate into neurons, AFSCs were injected into a neurogenic environment such as the telencephalon and cerebellum of newborn rats. Amniotic fluid was collected from women undergoing routine prenatal amniocentesis; AFSCs were isolated, cultured, expanded. Afterwards they were transfected with a lentiviral vector carrying the GFP (green Fluorescent Protein) gene, in order to be able to follow their survival. They were then maintained for 3 weeks in 2 different conditions: in a basal medium or in a Neuron Progenitor Maintenance Medium. The cells were then transplanted into the telencephalon and cerebellum of postnatal rats, in order to evaluate their neuronal differentiative potential. The cells were maintained in culture for 1 to 28 days (without growth factors) and then fixed.

We performed immunohistochemistry analyzes, focusing on the morphology and on the phenotypical characterization of the transplanted cells (in particular the expression of some neuronal and glial antigens, such as Nestin, Neu-N, Olig-2 and S-100 were examined). Morphological analyzes showed that some cells took on a neuronal morphology at very short times after the graft. Immunohistochemistry analyzes on these cells revealed that the origin of this phenomenon was not a neuronal transdifferentiation but probably a cellular fusion. Study and characterization of the AFSCs is a developing topic; experiments are going ahead to further delineate the role and the behavior of these cells when grafted into a neurogenic tissue.

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Adenosine receptor expression is higher in placentas of women with preeclampsia

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It is hypothesized that the pathophysiology of preeclampsia begins with shallow trophoblast invasion leading to placental hypoxia. Hypoxia is a potent stimulus for the release of adenosine. Women with preeclampsia and infants that are small for gestational age (SGA) show increased circulating concentrations of adenosine.

Objective: We tested the hypotheses that the adenosine receptor subtypes A1 A2A, A2B and A3 are expressed in the placenta, expression is higher in preeclamptic pregnancies and under in vitro hypoxic conditions.

Methods: Placental biopsies were obtained from primiparous women with uncomplicated pregnancies, preeclampsia or preeclampsia with SGA infants and SGA without preeclampsia. Placental villous explants were dissected and incubated for 24h at 2% or 20% oxygen. Adenosine receptors RNA and protein were determined by Western blotting, real time RT-PCR and immunocytochemistry. Data are presented as median fold changes compared to uncomplicated pregnancies. Statistical analyzes were performed with Wilcoxon-signed rank test. Probability values were considered significant at p<0.05.

Results: All adenosine receptor subtypes were expressed in human placenta. The protein expression of adenosine receptor subtypes A1 A2A, A2B and A3 was 1.52, 1.71, 2.52 and 2.36 fold higher in placental biopsies from preeclamptic women (N=6, p<0.05) compared to uncomplicated pregnancies, respectively. SGA pregnancies showed no difference in receptor expression. Real time RT-PCR confirmed these findings. In vitro hypoxia increased A2A-R 1.46 and 1.25 fold and HIF-1α protein 2.3 or 2.1 fold in villous explants of uncomplicated or preeclamptic pregnancies compared to 20% oxygen (N=6).

Conclusions: Our Results suggest a possible role for adenosine receptors in the pathophysiology of preeclampsia.

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Differential expression of VE-cadherin and flk-1 in the syncytiotrophoblast of preeclamptic placentas compared to healthy controls

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Objective: VE-cadherin is promoting intercellular adhesion of endothelial cells thereby regulating endothelial integrity and permeability. Moreover, VE-cadherin is involved in the regulation of Flk-1 receptor activity and thus cell cycle regulation. Preeclampsia has been associated with impaired syncytial function and altered trophoblast turnover. Therefore we investigated whether altered VE-cadherin and Flk-1 expression might be associated with preeclampsia.

Methods: Biopsies of placentas from 19 patients with late onset preeclampsia and 24 healthy term deliveries as well as 20 cases of early onset preeclampsia and 20 preterm controls were stained for VE-cadherin and Flk-1.

Results: All biopsies showed VE-cadherin and Flk-1 expression in placental vessels and in the syncytiotrophoblast. VE-cadherin expression in the syncytiotrophoblast was significantly higher in late onset preeclamptic cases and flk-1 expression was less pronounced compared to term controls. Whereas in early onset preeclampsia VE-cadherin was significantly less and flk-1 significantly more expressed compared to preterm controls.

Conclusion: Differential expression of VE-cadherin and Flk-1 might contribute to the etiopathologic events at the fetomaternal interface in preeclampsia. Since reduction of VE-cadherin and increase of flk-1 could lead to pronounced cell activation in the syncytiotrophoblast these changes than would enhance necrotic shedding instead of apoptotic shedding. The syncytial material released into the maternal system on necrotic shedding is believed to cause the maternal syndrome of preeclampsia. Thus overexpression of VE-cadherin and downregulation of flk-1 would represent a more stable situation in the syncytiotrophoblast and could possibly display a compensatory mechanism in the late onset cases.

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Endotoxin-induced chorioamnionitis is confined to one amniotic cavity in twin pregnant sheep


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Multifetal pregnancies have significantly increased since introduction of assisted reproductive technologies with an inherent risk of prematurity. Chorioamnionitis (CA) and respiratory distress remain the leading causes of perinatal morbidity and mortality. It is still not understood whether CA is restricted to a single amniotic cavity in multifetal pregnancies with impact in case of premature rupture of membrane (PROM) or suspected CA. We hypothesized that CA is restricted to a single uterine compartment and does not affect the neighboring fetus in twin pregnancies. We subjected fetal sheep via ultrasound-guided amniocentesis to the bacterial endotoxin lipopolysaccharide (LPS) injected to the amniotic fluid at gestational day 111. Six singletons were exposed to 10mg LPS and 5 singletons received saline for control. In twin pregnant ewes (n=6) one fetus received LPS and the other saline. Fetuses were delivered via c-section at 125 days. CA was verified via classical histology of the membranes meanwhile lung maturation was shown by pressure-volume curves of the lung. Inflammation of the membranes and the fetal lung where detected only after previous endotoxin injection. CA was limited to the amniotic cavity in which endotoxin was injected but the neighboring twin was unaffected. Lung maturation was induced by endotoxin injection with lung gas volumes of 42±8 mL/kg in comparison to 12±5 mL/kg in controls (p<0.05). No differences in lung maturation were observed between singletons and twin fetuses. This study may contribute to found a clinical trial in case of PROM and supposed CA for intentional delayed delivery in multifetal pregnancies.

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Identifying predictors of stillbirth and neonatal mortality in a UK population using graphical chain models

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Variations in stillbirth and neonatal mortality rates are known to exist between different populations. The reasons for this are not clear and the identification of potential influences on mortality is important to enable intervention to both reduce overall rates of mortality and to reduce inequalities between populations.

While conventional statistical modeling can be used to identify characteristics associated with mortality, it does not take into account the temporal and potential causal ordering of these potential explanatory variables. Graphical chain models have been proposed as a statistical method to allow the ordering of these characteristics to be specified in the model, identifying direct and indirect associations. This approach also allows the model to be displayed in a simple graphical form.

In this paper two graphical chain models are presented investigating stillbirth and neonatal mortality in a geographically defined UK population. The data were obtained from the Leicestershire Perinatal Mortality Study, a case-control study of stillbirths and neonatal death occurring to women resident in Leicestershire, UK. In this paper data on all stillbirths (excluding therapeutic abortions), neonatal deaths and control subjects from 1996 to 2005 were used. The data comprised 753 stillbirths, 537 neonatal deaths and 1732 controls.

Potential explanatory variables were categorised into inherent, prenatal, antenatal, and perinatal characteristics. The associations between the variables and between the variables and the outcomes were identified using the DIGRAM software.

These models offer insights into potential direct and indirect associations with stillbirth and neonatal mortality.

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Pregnancy-associated hypertensive disorders and adult cognitive function among Danish conscripts

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Background: Pregnancy-associated hypertensive disorders (gestational hypertension, preeclampsia, eclampsia) are a major cause of perinatal mortality and morbidity. There is little data on long-term neurodevelopmental sequelae of prenatal exposure to these disorders. We examined the relation of maternal gestational hypertension and preeclampsia with adult cognitive function in the offspring.

Methods: The study population consisted of Danish men born in 1978-1983 undergoing mandatory evaluation for military service. We ascertained conscripts’ birth data and maternal hypertensive disorders from population-based medical registries. Using Results of intelligence testing conducted at conscription, we examined the conscripts’ cognitive function according to prenatal exposure to pregnancy-associated hypertensive disorders.

Results: Of the 20244 men registered for conscription, 17812 (88%) had data on intelligence testing. Among them, 927 (5.2%) had been born after a pregnancy with recorded hospitalization for a gestational hypertensive disorder (1.7% for gestational hypertension and 3.5% for preeclampsia). Compared with conscripts born after normotensive pregnancy, the crude prevalence ratio for low cognitive function (IQ<85) was 1.28 (95% CI 1.01-1.62) among conscripts exposed to maternal gestational hypertension. For those exposed to mild and severe maternal preeclampsia, prevalence ratios were 1.20 (95% CI 1.00-1.43) and 1.44 (0.83-2.47) respectively. The corresponding crude mean differences (95% CI) in IQ scores were -1.6 (-3.5 to 0.2); -2.4 (-3.7 to -1.1); and -3.1 (-7.4 to 1.2). The associations were not explained by preterm birth or growth restriction.

Conclusion: Prenatal exposure to gestational hypertensive disorders is associated with reduced adult cognitive performance among male draftees.

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Screening for domestic violence in pregnancy-preliminary data from German maternity hospitals

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Violence against women by their intimate partners is an important public-health problem worldwide. Such violence is associated with a wide range of negative physical and mental-health outcomes among women. Domestic violence (DV) often continues- and at times starts-during pregnancy. Negative pregnancy outcomes associated with domestic violence include low birth weight, preterm labor, placental abruption, reduced levels of breast feeding. Poor attendance at antenatal clinics, poor nutrition and substance abuse are commonly observed in these settings. The Royal College of Midwives, the Royal College of Obstetricians & Gynecologists and the American College of Obstetricians and Gynecologists recommend routine screening at least three times during pregnancy. Studies in Germany are non-existent. This prompted us to investigate the prevalence of DV in three German maternity hospitals by routinely asking pregnant women attending antenatal clinics to fill out a questionnaire about DV. We furthermore screened for acceptance of implementing questions about intimate partner violence amongst our pregnant population.

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Intimate partner violence during and after pregnancy: Findings of the maternal health study

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Few longitudinal studies have investigated the prevalence of intimate partner violence during and after pregnancy, and associated health outcomes.

Methods: The Maternal Health Study is a multi-centre prospective pregnancy cohort study. 1507 nulliparous women completed a baseline questionnaire between 10-24 weeks gestation (initial response fraction =21%). Participants were followed-up at 3, 6, 9, 12 & 18 months postpartum. Response fractions at 3, 6 and 12 months were 95%, 93% and 90% respectively. Study instruments include standardized measures of urinary and faecal incontinence, depression and intimate partner abuse (Composite Abuse Scale).

Results: 5.1% and 5.4% of women were afraid of an intimate partner during pregnancy and in the first year postpartum respectively. One in six women (17%) reported physical and/or emotional abuse in first year postpartum (based on responses to the Composite Abuse Scale). Women who experienced abuse were more likely to be younger, unmarried, have a low income, not in paid employment in pregnancy, and to have had one or more terminations before this pregnancy. Women who were afraid of an intimate partner during pregnancy were more likely to report back pain, vaginal bleeding, anxiety, depression, severe urinary incontinence, and moderate or severe faecal incontinence in early pregnancy (mean gestation =15 weeks) compared with women who had never been afraid of any partner.

Conclusion: Fear of an intimate partner, before pregnancy or during the early stages of pregnancy, is associated with worse physical and psychological health in early pregnancy.

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Does neonatal weight gain mediate the association of early breastfeeding and childhood overweight risk in offspring of diabetic mothers?

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In normal populations, breastfeeding protects against obesity risk in later childhood, while rapid neonatal weight gain predisposes to it (1). In a cohort of 112 offspring of diabetic mothers (ODM) early neonatal breastfeeding (i.e. day 1 – day 7) dose-dependently increased overweight risk (2). Therefore, we now investigated whether breastfeeding may also be associated with an increased neonatal weight gain and a consequently increased overweight risk in the second year of life. Early neonatal ingestion of diabetic breast milk was positively associated with neonatal weight gain (β=0.41, p=0.047) and with relative body weight in the second year of life (β=0.32, p=0.004). Neonatal weight gain was positively associated with later overweight (odds ratio: 2.19, 95% confidence interval: 1.03-4.63). Adjustment for neonatal weight gain weakened the association between neonatally ingested amount of diabetic breast milk and relative body weight in childhood (β=0.28, p=0.001), while early body weight gain itself was significantly positively associated with later overweight (β=0.24, p=0.03). In summary, increased neonatal weight gain, induced by early neonatal ingestion of diabetic breast milk, may be a critical mediator in the relation between breastfeeding and childhood overweight risk in offspring of diabetic mothers (3).

(1) Stettler et al., Circulation 2005; 111: 1897-1903.
(2) Plagemann et al., Diabetes Care 2002; 25: 16-22.
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Teenage pregnancy outcome in Cambridge University Hospital (Rosie Maternity Hospital)

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Objective: The objective of the study was to evaluate the obstetric and neonatal outcomes of teenage pregnancy in a tertiary care teaching hospital.

Methods: A retrospective audit was performed over a period of one year (Aug 2006-Sept 2007). Data were retrieved from hospital records. All singleton pregnancies of teenage mothers (aged 13-19 completed years at delivery) delivering in the University Hospital were included.

Results: The incidence of teenage deliveries in hospital over 1 year was 3.1% (184). The majority of the teenagers were primigravida (73.2%). Incidence of smoking was 48% and alcohol misuse was 11%. Complications included pregnancy induced hypertension (PIH)/pre-eclampsia (PET) (3%), antepartum haemorrhage (APH 2%) obstetric cholestasis (2%), anaemia (2%), premature onset of labor (11%). Teenage mothers had increased incidence of low birth weight (LBW) (15%). The rate of caesarean section was 15.1% and instrumental delivery rate was 15.4%. Incidence of gastroschisis was 2.1%. There was no neonatal mortality though there were 28 NICU admissions immediately after delivery.

Conclusion: The Results indicate that the major risk associated with teenage pregnancies in our hospital was confined to preterm labor and low birth weight, but these were not associated with an adverse neonatal outcome. Good compliance with antenatal care, a relatively low incidence of social deprivation and the provision of high quality care by the multi-professional team may be factors associated with the favorable outcome in this population. Awareness of the risks in this population is useful for future service provision amongst this vulnerable group of women.

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Prevalence of gestational diabetes mellitus and gestational impaired glucose tolerance in 1653 adolescent pregnancies

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Objective: The increase in prevalence of childhood and adolescent obesity worldwide accompanied the conditions of insulin resistance. The aim of this study was to determine the prevalence of gestational diabetes mellitus (GDM) and gestational impaired glucose tolerance (GIGT) in adolescent pregnancies, associated risk factors and pregnancy complications.

Methods: Results of 1653 pregnant women ≤19 years between 2005-2007 were reviewed, retrospectively. All pregnant women screened with 50g glucose challenge test (GCT) and patients with a GCT Result ≥140mg/dl underwent 3 hour 100gr oral glucose tolerance test (OGTT). GDM was diagnosed with at least 2 abnormal Results and GIGT was diagnosed with one abnormal Result at OGTT.

Results: The prevalence of GDM was 0.85% (n=14) and GIGT was 0.5% (n=8) by Carpenter and Coustan criteria. 50% (n=11) of patients was overweight (body mass index ≥25), 59.1% had family history of diabetes and 31.8% had polycystic ovary syndrome (PCOS). Only 9.1% (n=2) of them required insulin for glucose regulation during pregnancy. Mean birth weight was 3532±372SD with 9.1% (n=2) macrosomia rate. 94.4% (n=21) delivered at term. All patients were primiparous and cesarean delivery rate was 27.3% (n=6).

Conclusion: We demonstrated that GDM and GIGT are conditions with increasing prevalence in adolescent pregnancies which are strongly associated with obesity before pregnancy, PCOS and family history of diabetes. Since GDM is a state of prediabetes, screening is important in adolescent pregnancies to take preventive measures.

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Perinatal mental health: Australian women’s experiences of psychosocial inquiry by primary care providers following birth

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Background: Australia has introduced a national perinatal mental health policy with a focus on routine screening. A survey of recent mothers explores women’s experience of psychosocial inquiry postpartum.

Methods: All women who gave birth in September/October in 2007 in two Australian states were invited to complete a survey six months post birth.

Results: Preliminary data (n=1992) show that 99% of women accessed primary health care providers in the six months postpartum. Forty-two percent of women reported three or more visits to a general medical practitioner (GP), 62% reported visits to a maternal and/or child health nurse. Many women were asked by a GP (46%) and/or nurse (65%) about physical recovery postpartum. Psychosocial inquiry was less common with 25% of women reporting a GP asked about depression and anxiety. Less than 5% were asked about other psychosocial issues, such as violence. Around half the sample were asked by a nurse about depression (57%) and anxiety (50%). Rates of inquiry by nurses about violence and drug/alcohol use were <20%.

A third of women (37%) reported dealing with at least one major social health issue since birth (i.e. serious family conflict, emotional abuse). At 5-6 months postpartum 28% of women experience anxiety, stress and/or depressive symptoms.

Conclusion: This population-based data provides a benchmark for evaluating progress in achieving improvements in recognition and disclosure of psychosocial issues in primary care settings. Repetition of the survey will be an important vehicle for evaluating outcomes of perinatal mental health policy.

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The influence of mode of delivery on the cranial MRI findings in the newborns

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Purpose: We sought to establish the influence of the mode of delivery on the frequency of intra and extra cranial haemorrhages in asymptomatic term neonates.

Methods:
- Term neonates were imaged within 48 hours of delivery using a 0.2T MRI scanner. A neonatal radiologist recorded the incidence of subdural or subgaleal haemorrhage and cephalhaematoma.
- Infants with subdural haemorrhage were re scanned at 4 weeks of age and followed up by a neonatologist.
- Obstetric details were recorded retrospectively.
- Statistical analysis used normal delivery as the baseline.
- Results:
  - Total 494 neonates imaged following normal delivery (n=269), ventouse (n=65), forceps (n=35), failed ventouse leading to forceps delivery (n=29), elective caesarean section (n=49) and emergency caesarean section (n=47).
  - 38 (7.7%) neonates had subdural haemorrhage. Of these, 19 had normal delivery, 8 ventouse (OR=1.96), 3 forceps (OR=1.23), 6 forceps delivery after failed ventouse (OR=3.4; p =0.02) and 2 emergency caesarean section (OR=0.38). All resolved by the 4 week rescan with no reoccurrence to date.
  - The distribution of subgaleal haemorrhage (n=18) and cephalhaematoma (n=11) followed that of subdural haemorrhage.
- Conclusion:
  - Clinically silent cranial haemorrhages occur commonly during the birth process and with higher frequency after instrumental deliveries. These resolve spontaneously within 4 weeks without detrimental effects. When a subdural haemorrhage is diagnosed after 4 weeks of age, causes other than birth injury must be considered.

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The status of the preimplantation embryo in Germany

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The current discourse on the status of the embryo was initiated in 2000 by the German Medical Association (Bundesärztekammer) when they published a draft for the legalization of the preimplantation genetic diagnosis (PGD). The compatibility of the PGD with the German legislation (German Constitution and Embryo Protection Act) were discussed. In our representative ‘bioethical field study’ we compared the views of experts (104 human geneticists, 147 gynecologists, 166 pediatricians, 294 midwives and 168 ethicists) and the general public (1017 interviews) on the beginning of human life and the status of the preimplantation embryo.

The majority of the general public (46.7%), gynecologists (54.4%) and pediatricians (46.4%) choose the moment of nidation as crucial boundary that marks the beginning of human life, whereas the majority of human geneticists (45.2%), midwives (62.9%) and ethicists (65.5%) voted for conception as the decisive point. The status of the preimplantation embryo was described as ‘cluster of cells with a need for special protection’ by the majority of the general public (31.8%) and gynecologists (40.1%), the majority of the human geneticists (39.4%), pediatricians (44.6%), midwives (36.7%) and ethicists (42.9%) favored the description of the embryo as ‘potential human being’.

The differences in the categorization of the beginning of human life are quite crucial within the expert groups. Surprisingly the views of all groups on the status of the preimplantation embryo differ from the assumptions underlying German legislation (Embryo Protection Act).

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Multifetal pregnancy reduction: An analysis of the current condition

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Objective: In Turkey, there are 106 licensed IVF-ET Centers now. Multifetal Pregnancy Reduction (MFPR) is carried out to reduce the maternal and perinatal morbidity and mortality associated with high order multiple gestation mainly related with Assisted Reproductive Technology (ART). The aim of this paper is to present MFPR experience from a single institution.

Methods: These patients were principally referred by infertility specialists from Ankara. The mean age of the patients were 27.95+ 7.1 and only 10% of the patients were 35. All of the procedures were performed in the first trimester (mean gestational age was 12 (+1) - 21 weeks). Trans-abdominal MFPR was carried in 187 cases of multiple pregnancy (twins 27 cases, triplets 103 cases, quadruplets 47 cases, and quintuplets 10 cases, and sextuplets 8 cases). Totally 344 fetuses were reduced.

Results: MFPR was accomplished in all cases (344/344 fetuses). None of the cases had blood coagulation disturbances. There were no cases of chorioamnionitis or other maternal complications. Results related to pregnancy outcomes after MFPR will be presented in the final manuscript.

Conclusion: Though MFPR is a procedure aimed to decrease the complications of multifetal pregnancy and increase the birth weight and seems not to interfere with the blood coagulation and the death of remaining fetus, the mean age of the patients and the excess number of embryos transferred in this report deserves consideration to think. Any practice that transfers more than one or two embryos, for instance due to commercial interests, should be abandoned.

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Structured decision process and documentation for termination of pregnancy on medical indication in the IIInd trimester

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Terminations of pregnancy (TOP) in the IIInd trimester pose a medical and ethical challenge to the couple and the staff. The process of diagnosis, decision and counseling should therefore meet the following features: state-of-the-art diagnostic accuracy, all procedures have to be according to national law and to professional guidelines, the patient has to achieve sufficient understanding of the diagnosis and of her own emotional and ethical values for “informed consent”. In cases of discordant ethical views concerning TOP dependent on the severity of the fetal condition, staff members will only identify with decisions, if they take part in a transparent decision process.

To achieve these aims, we held 4 staff discussions supervised by an independent psychotherapist. They yielded several major Results: All ambiguous cases have to be dealt with in formal staff meetings, before therapeutic alternatives may be suggested to the patient. Pertinent neighboring disciplines have to be consulted, non-clinical ethic committees don’t seem appropriate. Minority votes have to be heard, majority decisions ought to be respected. Clinical psychology is integral part of the counseling strategy. A 3-day moratorium between decision and TOP should be kept. Fetocide cannot be mandated. A final report should be given after all (discordant) cases of TOP in the staff meeting.

An electronic data sheet was devised, using ICD-10 diagnostic groups and categorizing the decision process and patient-doctor interaction.

Preliminary Results with this procedure have shown a very high rate of unanimous decisions and an improved acceptance of controversial issues.

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End-of-life decisions in the neonatal unit – a prospective study

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Introduction: Restriction of ongoing intensive care (RIC) is an alternative to (1) withdrawing/withholding intensive care to neonates (2) the practice of euthanasia. There are only few systematic studies on this issue.

Purpose: To study the practice of RIC in one single NICU

Methods: Using a structured record form with medical criteria and variables of ethical relevance, a prospective study on patients with intended RIC was done.

Results: 40 consecutive patients were recorded (25 preterms, 21 with a genetic defect or inborn malformation, 11 with intraventricular hemorrhage). RIC was (a) opted for in 32 patients; (b) discussed but not opted for in 4 patients; (c) not discussed in 4 patients, even though an ethical problem was claimed. RIC was applied as (n): no resuscitation (19), terminating (or refrain from) mechanical ventilation (16) or circulatory support (19). Basis for the decision was: extremely poor prognosis (13), deterioration with a very bad general prognosis (8), exhausted therapeutic options (5). The definite wish of mother or father was known in 77 and 72%, respectively, in 82% they were informed about the final decision. 6 patients were discharged home, 2 of them died later.

Conclusions: There is a broad spectrum of potential RIC measures that can be tailored to the individual situation of the patient and the parents' wishes. The role of parents between "comprehensive informed consent" and "complete involvement" seems worth discussing.

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Neonatal organ donation – opportunities and limitations

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Until recently, organ donation in Australia was only possible after declaring brain death, precluding neonates from donation. Change in legislation and development of guidelines for donation after cardiac death have been developed in NSW/ACT over the last 2 years. Two female infants were born by emergency caesarean section following a placental abruption, and developed multiorgan failure following severe perinatal asphyxia. The first infant (28 weeks, bw 1210g) developed extensive bilateral IVH IV with ventricular dilatation on day 2, the second infant (37 weeks, bw 2495g) had evidence of extensive cerebral damage on MRI. Palliative care was offered to both neonates and both sets of parents requested consideration for organ donation. Following liaison with the organ donor coordinators as well as with the Queensland Heart Valve Bank and NSW organ donation centre, LifeGift NSW/ACT, both infants were accepted as donors. The first infant donated heart valves. Parents of the second infant gave consent for liver donation, but as there are no neonatal guidelines for cold ischaemia time, adult guidelines were followed and the donation could not occur. The baby only donated heart valves.

A further change in legislation may make neonatal solid organ donation possible. Nationally, 41 children are awaiting organ transplantation, which strengthens the need for the development of guidelines for donation in children and neonates. Neonatal guidelines need to take into account differences in physiology, resistance to hypoxia and possible increased cold ischaemia time for solid organs. In addition, ethical concerns need to be addressed.

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Influence of nausea and vomiting during pregnancy in women’s psychological health:
An alternative proposal

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Nausea and vomiting during pregnancy can alter the clinical condition of the pregnant woman. Several investigations have highlighted the contribution of psychological factors in the development of this symptomatology, although its role it’s unclear.

Objective: Analyze the association between personality traits and psychological clinical symptoms with nausea and vomiting. Propose an explanatory model of the effect of nausea and vomiting over psychological symptomatology in pregnant women.

Methodology: Correlational retrospective design. A sample of 196 pregnant women from the Comunidad de Madrid were selected. They were recruited telephonically after the first trimester ultrasound.

The following instruments were used: NEO-FFI: to evaluate the big five personality traits. SCL-90-R: to assess psychological clinical symptoms. NVPI: to assess nausea and vomiting.

A regression model was established using as dependent variables the symptomatology subscales of the SCL-90-R, and entering subsequently sociodemographic variables, HCG, NVPI scores and NEO-FFI scores.

Results: A statistically significant effect is found for nausea with an important influence of neuroticism.

- Depression: Adjusted $R^2$ of 0.487, nausea $\beta=0.161$ p=0.003, neuroticism $\beta=0.715$ p<0.001.
- Anxiety: Adjusted $R^2$ of 0.485, nausea $\beta=0.121$ p=0.025, neuroticism $\beta=0.713$ p<0.001.
- Somatization: Adjusted $R^2$ of 0.428, nausea $\beta=0.415$ p<0.001, neuroticism $\beta=0.446$ p<0.001.
- Obsession: Adjusted $R^2$ of 0.369, nausea $\beta=0.121$ p=0.041, neuroticism $\beta=0.623$ p<0.001.

Conclusions: Nausea and vomiting during pregnancy may lead to psychological disturbances in pregnant women, this risk can be increased in the presence of high scores in neuroticism.

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The impact of pain experience in a woman’s history on delivery

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Design: Within a multi-step study (including 1000 pregnant women, 5 measurements are taken: pre-during- post delivery: immediately after, after 3 and 6 months) a hypothesized correlation between anxiety (fears) and pain during delivery is evaluated.

Method: Previous traumatic experiences and anxieties concerning their upcoming delivery are asked for in a half-standardized questionnaire and by the SSG during the first contact in a prepartum walk-in. 230 pregnant women have already been interviewed and observed in delivery. 14.8% had a history of physical violence including sexual abuse and torture. Concerning the anxieties during pregnancy 4 categories were differentiated:

- injury of one’s own body,
- injury of the child during the delivery,
- disability of one’s child
- other fears to be specified.

Results: For all women with and without violence experience the dominant fear is the injury of the child during delivery (83%).

In case of physical violence and sexual abuse fears in all 4 categories were equally prevalent. Women without any violence and pain experience show a remarkable gap between the expected pain during delivery and the finally experienced pain and get overwhelmed.

The correlation of expected and experienced pain is especially distinctive in women with previous physical pain experience and influences the delivery in duration, mode of delivery and medical interventions.

Discussion: The vicious circle of anxiety driven modulation of pain should be cut through by pre-partum psychosomatic strategies and adequate pain treatment during deliveries.

Women with no pain experience have to be more carefully prepared for their deliveries in order to have better coping strategies at hand.

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Personality traits and depressive symptomatology as predictors of postpartum depression

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Introduction: Around 10-15% of women suffer from postnatal depressive disorder. Factors such as pain catastrophizing, previous depressive symptomatology or neuroticism can increase the probability of development of postnatal depression.

Objectives: To analyze the relationship between depressive symptomatology in early pregnancy and postnatal depression. To analyze the effect of personality traits in the development of maternal depression. Methodology: Longitudinal correlational prospective design. Sample composed of 62 women from the Comunidad de Madrid, selected after the first trimester ultrasound and followed until 4 months after delivery. Instruments: NEO-FFI: to evaluate the big five personality traits. SCL-90-R: to assess psychological clinical symptoms, only the depression subscale was used in this study. EDPS: to evaluate postpartum depression. Results: Women working at the beginning of pregnancy showed statistically significant higher scores in EDPS scale than women not working (t=2.14; p=0.036). A statistically significant positive correlation was found between EDPS scores and SCL-90-R depression scores (Pearson’s r=0.401; p=0.001) and neuroticism (Pearson’s r=0.449; p=0.000) in early pregnancy, and a negative significant correlation with conscientiousness (Pearson’s r=-0.348; p=0.006). Multivariate analysis of postpartum depression found significant effects of neuroticism (R² of 0.202; neuroticism β=0.426 p=0.021). Multivariate analysis of postpartum depression found significant effects of conscientiousness and depression (R² of 0.214; conscientiousness β=-0.313; p=0.014 and depression β=0.336; p=0.012). Conclusions: Women showing high scores in neuroticism, low scores in conscientiousness or depressive symptomatology in the first trimester of gestation should be carefully monitored through pregnancy and postpartum to facilitate early detection of this disorder.

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Obstetric brachial plexus palsy: The challenge for interdisciplinary cooperation and the
Results from reconstructive microsurgery

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Obstetric brachial plexus palsy is a rare but sometimes severe nerve injury impairing main motor and
sensitive function of the affected upper limb. Risk factors as shoulder dystocia, macrosomia, breech
presentation and traction maneuvers are known; but the treatment strategy and outcome in severe
upper and total plexus palsies remains unknown within the community of obstetricians. Furthermore,
the discussion about the etiology and pathophysiology of these lesions remains controversial.
We present a common approach model for both obstetricians and plexus surgeons; explain the
actual knowledge about traction forces related to peripartal nerve injuries and show outcome Results
in babies with severe lesions.
The medico-legal issue could take benefit from a common approach which clearly outlines the
characteristics of difficult birth and the treatment modalities in obstetric palsy.

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Perinatal circulating surfactant protein D concentrations in intrauterine growth restriction

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Background: Collecting surfactant protein D (SP-D) is an important component of the innate immune system and upregulated in pulmonary disease. Intrauterine-growth-restricted-(IUGR) neonates may present with structural lung immaturity, impaired immunocompetence and increased risk for respiratory infections and chronic obstructive lung disease in later life.

Aim: To investigate circulating SP-D concentrations in maternal, fetal and neonatal samples from IUGR and appropriate-for-gestational-age-(AGA) pregnancies. Methods: Circulating SP-D concentrations were determined in 40 mothers and their 20 IUGR and 20 AGA singleton full-term fetuses-neonates on postnatal day 1-(N1) and 4-(N4).

Results: Fetal SP-D concentrations were higher in IUGR group (b=18.16, p=0.002, 95% CI: 6.86-29.47) and negatively correlated with infants' customized centiles and gestational age (r=-0.326, p=0.04 and r=-0.446, p=0.004, respectively). In both groups, maternal SP-D concentrations were lower than N1 and N4 ones (p≤0.001 in all cases), and fetal SP-D concentrations were lower than N1 and N4 ones (p≤0.015 in all cases). N1 SP-D concentrations were higher in vaginal deliveries (p=0.032).

Conclusions: Higher fetal SP-D concentrations in IUGR may reflect early lung injury, leading to increased alveolar-vascular permeability and protein leakage into the circulation, or accelerated lung maturation due to intrauterine glucocorticoid exposure, Resulting to increased SP-D production. SP-D concentrations postnatally increase and are higher in neonates born vaginally, probably due to lung liquid reabsorption during the start of respiration and delivery stress, respectively. A progressive decrease in placental function Results to downregulated SP-D production, accounting for negative correlation between fetal SP-D concentrations and gestational age.

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Perinatal changes of circulating clara cell protein concentrations in pregnancies with normal and restricted fetal growth

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Background: Clara cell protein (CC16) is an immunomodulatory/anti-inflammatory broncho-alveolar-derived molecule and a biomarker of pulmonary epithelial cells maturity and alveolocapillary membrane injury. Intrauterine-growth-restricted-(IUGR) neonates may present with structural lung immaturity, impaired immunocompetence and increased risk for respiratory infections and chronic obstructive lung disease in later life.

Aim: To investigate circulating CC16 concentrations in maternal, fetal and neonatal samples from IUGR and appropriate-for-gestational-age-(AGA) pregnancies.

Methods: Circulating CC16 concentrations were determined in 40 mothers and their 20 IUGR and 20 AGA singleton full-term fetuses-neonates on postnatal day 1-(N1) and 4-(N4).

Results: No significant differences in CC16 concentrations were observed between IUGR and AGA groups. In both groups, maternal CC16 concentrations were lower compared to N1 and N4 ones (p<0.001 in each case). Furthermore, fetal CC16 concentrations were significantly lower compared to N1 and N4 ones (p<0.001 in each case), while N1 CC16 concentrations were significantly higher than N4 concentrations (p<0.001). N1 CC16 concentrations positively correlated with gestational age (r=0.364, p=0.021). Finally, the effect of gender, parity and maternal age on CC16 concentrations was not significant. Conclusions: Lack of difference in CC16 concentrations between IUGR and AGA groups possibly suggests that the lung immaturity and later respiratory diseases associated with the former may not be related to early CC16 deficiency. CC16 concentrations increase with increasing gestational age and peak on the first day of life, possibly indicating a vital role of the protein in fetal lung maturation and acute extrauterine pulmonary adaptation.

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Fetal sympathetic nervous activity during the second trimester of pregnancy

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Introduction: Valuable information for assessing fetal wellbeing might be obtained from spectral analysis of fetal heart rate variability. In literature, spectral analysis of fetal heart rate has been reported only for pregnancies >20 weeks of gestation. The development of a non-invasive fetal ECG device has enabled the recording of the beat-to-beat fetal heart rate in pregnancies of 18 weeks of gestational age (GA) and higher. To investigate fetal sympathetic nervous activity in the second trimester of pregnancy, the beat-to-beat fetal heart rate was recorded in pregnancies of 18-27 weeks of gestation.

Methods: Measurements were performed in 50 healthy pregnancies using a prototype non-invasive fetal ECG device (NEMO). From these recordings R-R interval series were obtained and analyzed using Wavelet packets. Spectral powers were calculated in the very low frequency (VLF) band (<0.04 Hz), the low frequency (LF) band (0.04-0.15 Hz), and the high frequency (HF) band (0.4-1.5 Hz). In addition, normalized low (LFn) and high (HFn) frequency powers were calculated, as these may reflect autonomic nervous activity more objectively.

Results: In the period before 20 weeks of gestation, LFn is found to be significantly lower than in the period after 20 weeks of gestation (<20 weeks GA: LFn =0.39±0.20, >20 weeks GA: LFn =0.74±0.15, p<0.001).

Discussion and Conclusion: The significantly lower normalized LF power for gestational ages <20 weeks might indicate that functional development of the fetal sympathetic nervous system does not take place earlier than 20 weeks of gestation.

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Detection of fetomaternal haemorrhage with a particle gel immunoassay

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Determination of fetomaternal haemorrhage (FMH) remains an area of difficulty. In most cases, prophylactic Rh immunoglobulin is usually administered to affected women without testing for fetal red blood cells (RBC). Here, we describe a new particle gel immunoassay (PaGIA) for the determination of FMH (FMH-PaGIA). Superparamagnetic particles were coated with monoclonal anti-D and mixed with ethylenediaminetetraacetic acid-anticoagulated blood samples from D-negative pregnant women. The particles were isolated using a magnetic particle concentrator and then placed into the reaction chamber of a gel card. Agglutinated particles on top or dispersed through the gel matrix indicated the presence of D positive cells. After the test was adapted to detect 0.3% D-positive RBC, randomly selected postpartum samples from 208 women were analyzed in parallel with the Kleihauer–Bethke test (KBT). In addition, all discrepancies were further analyzed by flow cytometry. A total of 203 of the 208 postpartum samples were negative in both tests. One sample reacted positive with both assays. Two samples were strongly positive in the new FMH-PaGIA, but negative in the KBT. A serological re-examination revealed that both women were D positive. The KBT gave a false-positive result in two cases because of hereditary persistence of haemoglobin F. The new test is specific, easy to perform and can be done at any time in all laboratories.

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Influence factors on symphyseal joint width

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Symphyseal separation is a physiological change of the pregnant pelvis to facilitate vaginal delivery. Increased diastasis of more than 10mm can cause pregnancy-related pelvic girdle pain. There is few data about factors that influence the width of symphyseal joint in pregnant women.

Material and Methods: Sonographic width of symphyseal joint was measured in pregnant women before and after the onset of labor. All of them underwent ultrasound examination by two obstetricians who received a special training for measurement of symphyseal joint. Routine ultrasound before the onset of labor was added by three-dimensional ultrasound when available. Results were correlated to obstetrical data such as gestational age, multiple pregnancy, body mass index, regular labor or fetal presentation.

Results: Measurement of symphyseal joint was performed in 472 cases with altogether 420 pregnant women included, 64 measurements were done after the onset of labor. Median of symphyseal joint was 5.8mm with a 25th percentile of 4.8mm and a 75th percentile of 6.8mm before, and 6.8 m (5.8 and 8.5mm, respectively) after the onset of labor. After multivariate analysis, gestational age, multiple pregnancy or fetal presentation did not have a significant influence on symphyseal joint width. Body mass index at the time of measurement and parturition did have an influence on symphyseal joint width with higher values in obese women and women in labor.

Conclusion: Symphyseal joint width depends on maternal body mass index and is physiologically increased after the onset of labor.

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Effect of antenatal betamethasone treatment on neonatal stress reactivity

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There is evidence that antenatal corticosteroid treatment of women at risk for premature delivery may have a lasting impact on the functioning of the hypothalamo-pituitary-adrenal (HPA) axis in the infant. We analyzed postnatal stress regulation in healthy neonates that received antenatal betamethasone treatment.

Salivary cortisol and cortisone levels in 23 healthy neonates born >34 weeks of gestation with antenatal betamethasone treatment (2 doses of 12mg i. v., 24h apart) (mean treatment-delivery interval 60 days) was analyzed. Baseline levels and stress response after the heel-prick test as stressful event were compared with 40 untreated neonates.

Median gestational age at birth (266 vs. 273 days, p=0.2) and median birth-weight (2,950g (39. perc.) vs. 3,288g (52 perc), p=0.27) was comparable between treatment and control group, respectively. Median baseline levels for cortisol and cortisone were not significantly different between the treatment- (1.4ng/ml and 14.8ng/ml, respectively) and the control group (1.2ng/ml and 11.4ng/ml, respectively) (n. s.). In the control group, salivary cortisol and cortisone significantly increased 20 minutes after the stress induction (p<0.05). In contrast, neonates with antenatal betamethasone treatment exhibited a blunted steroid release after stress induction for cortisol and cortisone (p=0.76, p=0.69, respectively). No influence of neonatal weight, gestational age, gestational age at betamethasone treatment and gender was observed in a multiple stepwise regression.

Antenatal betamethasone treatment in pregnancies at risk for preterm delivery before 34 weeks of gestation appears to alter the physiological activity of the HPA axis in healthy neonates.

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Correlation between the maternal serum ferritin at third trimester and fetal growth

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Objective of this study was to determine the relationship between maternal serum ferritin at third trimester and fetal growth.

All cases were evaluated prenatally between Jan 2008 and February 2009 by prospective cross sectional study and were delivered in Kangwon National University Hospital. Inclusion criteria was full term singleton pregnancy without prenatally and postnatally congenital anomaly. Serum ferritin concentrations were measured at third trimester gestation in 131 cases. Exclusion criteria were preterm labor (13 cases), fetal anomaly (3 cases), Fetal death in utero (FDIU)(1 case) and multiple pregnancy. All cases were not maternal smoker. Among 131 infants, 114 were analyzed. Mean maternal age was 30.7±4.4 years (20 - 42 years). Birth-weight was 3.20±0.45kg (1.74 - 4.45kg). Mean gestation age was 38.9 weeks (37.0 – 41.4 weeks). Mean serum ferritin concentration was 33.16ng/mL (4.44 -367.80ng/mL). This group was divided by serum ferritin concentration ng/mL. In lower 30ng/mL group, birth weight was 3.26±0.47kg but in upper 30ng/mL group, birth weight was 3.07±0.38kg. This Result was significant in statistics. (P<0.05). But correlations were not significant between maternal serum ferritin at third trimester and neonatal birthweight. (P>0.05) Also, relationship between maternal serum ferritin and intrauterine growth restriction was not significant. (P>0.05)

Our conclusion was that high maternal serum ferritin levels may be associated with neonate birthweight. It was suggested that maternal serum ferritin was associated with fetal growth.

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Weight gain during pregnancy and fetal sex

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Objective: The recommendations of the Institute of Medicine (IOM) for weight gain during pregnancy – which depend on the BMI – are more and more used in Germany. We evaluated the real weight gain during pregnancy of 532 healthy women at term. Furthermore we investigated how far the real weight gain during pregnancy corresponds to the IOM-recommendations. In addition we assessed the correlation between weight gain and fetal sex.

Method: Retrospective, quantitative cross-sectional-analysis. Women filled out a self administered questionnaire 2-4 days after birth. Data of weight gain during pregnancy were taken from the official pregnancy record.

Results: The pregnant women gained 15.2kg on average. Less than half of the women (42.4%, n=221) fulfilled the IOM-recommendations. Women who gave birth to a girl (n=247) gained 14.61kg on average (SD=5.7), women who gave birth to a boy (n=276) 15.71kg (SD=6.38). Women who didn’t want to know about the fetal sex until birth showed significantly less often (p=.004) an increase in weight above the IOM-recommendations.

Conclusions: The Results indicate that it is necessary to develop recommendations for weight gain during pregnancy which take into account the individual physiological and psychosocial aspects. Further studies should investigate antenatal knowledge of male fetal sex as predictor for more weight gain in relation to the BMI and to the IOM classification.

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Chronic influence of small alcohol mother's doses on structural and metabolic features of the brain and liver of progeny: an experimental study in rats

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The use by young women of low-alcoholic drinks is a widespread habit. The aim of the investigation is to study action of chronic weak alcoholization of pregnant female rats on brain and liver structure and metabolism in them newborns. These rats were treated by a small daily dose (0.5g/kg) of ethanol water solution intragastrically. We have carried out histological research of liver and brain, biochemical research of γ-glutamintransferase, catalase, peroxidase activities and of diene conjugates maintenance in newborn's liver and brain.

We found out disseminated fatty degeneration of the hepatocytes, single cells with cytoplasm coagulation, macrophage-lymphocytic infiltration around portal tracts (prenatal chronic persisting hepatitis). The brain cortex of newborns was thinner, than in the control group; foci with neurons absence were found; the neurons size of 5th layer of cortex cerebri was reduced; the distance between neurons was increased (prenatal hypoplasia and atrophy of cortex). Increased γ-glutamintransferase, catalase, peroxidase activities take place in liver and brain tissues. Quantity of diene conjugates is increased in liver tissue and is decreased in brain tissue. The biochemical data explain development of a histologic picture of newborn liver and brain by prenatal alcoholic damage of biomembranes. The damage of newborn brain appeared stronger, than damage of liver, due to chronic low alcoholization during pregnancy.

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Postpartum depression and infant’s outcome – an interdisciplinary screening and 18 weeks follow up

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Introduction: Prevalence of depressive disorder after childbirth is about 10%. A significant amount cannot be detected. All the more, depressive disorder has an immense impact not only on mothers and the whole family but especially on the cognitive and mental development of the newborn. At present there are few interdisciplinary studies, from either the obstetric, pediatric or even infant psychiatric side.

Method: More than 700 women post partum, mean age 15-44 years, were screened at six points in time from the second day to the 18th week post partum by Edinburgh Postnatal Depression Scale (EPDS). High scoring women underwent the Structured Clinical Interview for DSM IV (SKID-I) to confirm diagnosis. Together with their infants, affected mothers were examined with a standardized videotaped mother-child interaction task.

Results: We found more than 10% scored highly on EPDS at any point during the first four weeks and about 6% scoring high on EPDS at more than two points in time during 18 weeks postpartum. During the 18 week period, 3-4% could be classified as suffering from depressive disorder according to DSM-IV/ICD-10 confirmed by SKID-I.

Discussion: Detecting postpartum depression is crucial. The EPDS questionnaire screening is suitable, is well accepted by the women, and should be recommended for every woman after childbirth. Certain patterns of high scoring EPDS have to be followed by a specific interview to implement early diagnosis and to offer specific therapy, focusing on both the mothers and the early mother-child attachment.

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Neurodevelopmental outcome in the third year of life after intrauterine laser coagulation for severe twin-twin-transfusion syndrome

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Objective: To evaluate the neurodevelopmental outcome in three consecutive groups of patients after intrauterine laser coagulation for severe twin-twin-transfusion syndrome (TTTS).

Patients and Methods: All patients received prenatal treatment in Hamburg and follow-up examinations in Bonn. 89/89 survivors of the treatment period Jan 95 – May 97, 167/172 from June 97 – Sept 99 and 128/179 from Jan 04 – Sept 06 were evaluated in their third year of life by standardized neurological examinations and neurodevelopmental tests.

Results: Data are summarized in the table. Survival after laser coagulation as well as developmental outcome improved significantly from the first to the latest time period.

Conclusion: There is evidence from these data that improvement in survival after intrauterine laser coagulation for severe TTTS is accompanied by improvement in neurodevelopmental outcome in the third year of life.

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Neuromotor outcome of very low birth-weight infants during the first year of age investigated by the Hammersmith infant neurological examination

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Background: The Hammersmith Infant Neurological Examination is a simple and scorable method for assessing infants between 2 and 24 months of age.

Objective: The purpose of this prospective study was firstly to evaluate the neuromotor outcome of very low birth weight infants during the first year of age; secondly to correlate the scoring of this neurological tool with brain ultrasound scans.

Methods: A total of 219 infants were enrolled from a level III Intensive Care Unit. Inclusion criteria were a gestational age \( \leq 32 \) weeks, a birth-weight \( \leq 1500 \)g, and absence of congenital disease. All infants underwent brain ultrasound between 36 and 40 weeks corrected age. The Hammersmith Infant Neurological Examination was performed at 6 and 12 months corrected age.

Results: Infants had a median (range) gestational age and birth weight of 28.6 weeks (24.6-32) and 1070g (570-1490), respectively. The global scores at 6 and 12 months corrected age had a median (range) of 65 (37-77) and 72 (31-78), respectively. There was no significant difference between brain ultrasound findings and the global score at 6 and 12 months corrected age but there was significant difference between periventricular leukomalacia and global score at 6 months (p=0.026).

Conclusions: The use of a standardized neurologic optimality scoring system could give additional prognostic information, easily available in the clinic, on the neuromotor outcome in very low birth weight infants.

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Comparison of findings on serial cranial ultrasound and routine magnetic resonance imaging at term in very low birth weight infants

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Objective: To compare findings of cranial ultrasound (US) and magnetic resonance imaging of the neonatal brain (MRI) obtained at term in preterm infants.

Methods: All our premature infants with a very low birth weight (VLBW) of less than 1,500 grams (period: 2004 to 2008) underwent cranial ultrasound scans on day 1, 3, 7, 14, 28, 42, monthly thereafter and at term corrected age. In addition they had a MRI of the neonatal brain at term. Retrospectively, we compared the cranial US findings as a predictor of a wide spectrum of pathology on MRI.

Results: paired MRI and US studies were performed in >200 VLBW infants who were born at a median gestational age of 29 (range: 22+1 to 34+5) weeks and a median birth weight of 900 (range: 335 to 1495) grams.

US predicted some MRI findings accurately: germinal layer hemorrhage (GLH), cystic lesions, intraventricular hemorrhage (IVH) and severe white matter (WM) echogenicity on US for the presence of WM hemorrhagic parenchymal infarction on MRI. Other MRI changes were less well-predicted: delay in maturation and myelination, reduced cortical folding, congenital malformations and mild or no WM echogenicity on US for the presence of normal WM signal intensity on MRI.

Conclusion: US predicted the presence of GLH, cystic lesions, IVH, and hemorrhagic parenchymal infarction on MRI. High-resolution imaging of the neonatal brain might shed light on the origin of brain lesions causing long-term neurodevelopmental sequelae in the preterm infant.

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**Long-term follow-up of children with prenatally diagnosed agenesis of corpus callosum (ACC)**

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Objective: The complete or partial absence of the corpus callosum has an incidence of 0.3%-0.7%. There are both a variation in outcome between asymptomatic appearance and severe neurologic problems and a lack of clinical data to counsel concerned couples. Aim was to study the outcome and follow-up of pregnancies with prenatally diagnosed ACC.

Methods: Maternal, neonatal, and pediatric records of prenatally diagnosed central nervous system (CNS) malformations in a tertiary referral center were reviewed over a 14-year period (1995-2008). Prenatal findings were compared with postnatal diagnosis, made either at autopsy, or a combination of imaging (sonography/MRI) and clinical follow-up. Information on current outcome was assessed by scored neurological examination.

Results: 24/241 fetuses diagnosed with a CNS malformation had an ACC. Complete ACC occurred in 18/24 (75%). A total of 46% (11/24) were isolated. Associated anomalies include microcephaly, spina bifida, and Dandy-Walker complex. A total of 21% (associated with structural/chromosomal abnormalities) were terminated. 79% of pregnancies (19/24) resulted in live births. Follow-up was available in 17 children. Psychomotor development was normal or slightly/moderately disabled for 80% (8/10) of children with isolated lesions. 5 out of 7 children with associated malformations are severely disabled/retarded and suffer from developmental delay, seizures, or cerebral palsy. These findings are nonrelated to complete or partial ACC.

Conclusions: The prognosis depends on associated malformations. The best prognosis occurs if ACC is isolated, although significant neurodevelopmental delay develops also in a consistent proportion of isolated cases. Knowledge from own study group and its follow-up combined with data from the literature leads to better counseling about the likely outcome.

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Follow-up of infants with total injury of the brachial plexus and erb palsy

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Introduction: Injury of the brachial plexus consists in inadequacy or palsy of the muscles in the upper limb which take innervation from the cervical roots C5-C8 as well as T1. The most usual type of injury is Erb injury of the upper part of the plexus.

Aim: Evolution of infants with total brachial plexus palsy and Erb palsy 6 months after diagnosis.

Material-Methods: 8 infants (6 boys, 2 girls) which were born in our hospital the period 1999-2008 (at a total of 8,126 deliveries at that period) showed adduction and internal rotation of the arm, missing pronation of the forearm, absent Moro reflexes at the affected side as well as biceps reflex, grasping reflex present. The infants were born with normal delivery, were overweight and had shoulder dystocia. 5 among them suffered from Erb palsy and 3 had total brachial plexus palsy.

Partial immobilation of the affected side was done – with the arm in such position to avoid development of shortening and abnormal contracture of the muscles – kinesitherapy, as well, and a follow-up 6 months later was performed.

Results: On re-examination 6 months later, infants with Erb palsy had shoulder, wrist and hand function within normal limits. Infants with total brachial plexus palsy improved the mobility of the hand but remained in supination of the forearm and complete extension of the elbow and shoulder.

Conclusions: Brachial plexus injury despite its variety has enormous social and practical consequences and pediatricians need to know thoroughly its natural history and treatment.

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Changes in survival and neonatal morbidity in infants with a birth weight ≤750 gram

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Objectives To describe the obstetric history and obstetric complications of women delivering infants with a birth weight ≤750 gram (g). To compare these variables between two consecutive five year periods and between small for gestational age (SGA, <p2.3) and appropriate for gestational age (AGA, ≥p2.3) infants. The question was raised whether being born with a birth weight ≤750 g can be prevented.

Methods A retrospective cohort study of 272 infants with a birth weight ≤750g and gestation of ≥24 weeks, born in 1996-2000 (cohort I, n=151) and 2001-2005 (cohort II, n=121), assessing maternal characteristics and neonatal outcome.

Results In 84.4% of the multigravids a complicated obstetric history was found; 44.5% had spontaneous abortion(s) and 24.2% a preterm delivery. In the index pregnancy the most prevalent obstetric complications were hypertensive disorders (52.1%, more in cohort II p<0.001), intrauterine growth retardation (IUGR) (80.8%, more in SGA infants p<0.001) and fetal distress (40.2%).

Conclusions Only 15.6% of our maternal population delivering infants with a birth weight ≤750g had an uncomplicated obstetric history. The most prevalent obstetric complications in the index pregnancy were pregnancy related hypertensive disorders and concomitant placental insufficiency and intrauterine growth retardation, whereas the prevalence of a spontaneous preterm birth occurred in a minority. We conclude that birth of infants with a birth weight ≤750g can rarely be prevented.

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Sepsis in obstetrics: Use of an early warning score and sepsis bundles

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Background: We've been using a Modified Early Warning Score System (MEWS) and sepsis bundles in obstetrics for five years based on the Surviving Sepsis campaign recommendations for three. We wanted to establish whether the MEWS charts detected and predicted the deterioration of patients due to sepsis, and if the bundle guidelines were adhered to.

Methods: A retrospective audit of all HDU admissions with the diagnosis of sepsis.

Results: Six women were admitted to HDU due to sepsis, 0.18% of births. All scored on two or more on the Criteria for Systemic Inflammatory Response Syndrome, three meeting the criteria for severe sepsis. 50% were post caesarean section (unit CS rate 25%). The heart rate in the patients was abnormal with readings between 108-195 (mean 141.83). Respiratory rate was normal in two patients abnormal in two (30-36) and not recorded in two. The temperature of three patients ranged from 39.1 to 40.1 and was normal in three. Five patients were normotensive and one hypotensive. All had broad-spectrum antibiotics, fluid resuscitation and blood cultures. Three had Serum Lactate levels checked. None required inotropic support. MEWS charts were started after patients becoming unwell, and hence did not add to single parameter observations in detection of severe sepsis. MEWS was useful in monitoring the response to treatment of these patients.

Comments: Severe sepsis is rare after childbirth. Tachycardia was the most useful criterion in detection. We could not show MEWS was better. More work is needed on the validity of MEWS in obstetrics.

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Long-term outcome of extremely preterm (ELBW) infants in Lower Saxony

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Objective: Information on long-term cognitive and neurological consequences of ELBW and their relevant factors of influence is scarce.
In the federal state of Lower Saxony a long-term outcome-project, which is unique in Germany, analyzes prospectively the neurodevelopmental outcome at defined follow-up intervals. All departments of neonatology and all divisions of pediatric neurology are participating. On the basis of these Results an improvement of neonatal medical care and quality of life can be reached.

Methods: The project includes children who were born at <28 weeks’ gestation. A long-term scheme (6 months, 2 – 5 – 10 years) of standardised examinations (for example Bayley 2 mental scale) is established. The Results of the long-term study are correlated to data of perinatal and neonatal quality assurance measures.

Results: 430 children (born 2004-2007) were examined at the age of 6 months and 255 children (born 2004-2006) at the age of 2 years. After 2 years 21% of the children show a major impairment, 39% a minor impairment and 40% a normal development.

Comparison with Results of the 6-month-examinations (11% with major, 44% with minor impairment and 45% normally developed) shows the importance of systematic examinations at defined ages. So necessary therapies can be introduced immediately (e.g. before entering nursery school or primary school).

Conclusions: A follow-up rate of 85%, even after 2 years, confirms the prospective study concept supported by central monitoring.
The study improves the co-operation (networking) of the different professions (pediatrics – neonatology - developmental support) carry ELBW infants and long-term outcome.

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The problem of virus-bacterial infections in obstetrics pathology

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Study of features of current and outcomes at virus and bacterial infections at the women, development of rational tactics of running of pregnancy, delivery at the women and newborn. We have revealed 2900 pregnant women with virus and bacterial infections: virus hepatitis B and C, herpes, cytomegalovirus, chlamydia, HIV infection and followed them during pregnancy. The verification of the diagnosis was carried out in view of the data clinical and special methods of researches. The medical therapy directed on removal of symptoms most frequently to an observed pathology, with the account thus of a degree of weight and stage virus hepatitis, has allowed to keep pregnancy at all women. To prevent development of virus hepatitis B all newborns were introduced vaccine and immunoglobulin during the first hours after delivery, and following vaccination of 1, 2 and 12 months of life. With the purpose of preventive maintenance virus hepatitis C applied immunoglobulin. At display of clinical symptoms of an infection to children carried out antivirus and symptom therapy, detailed virology research, with the subsequent supervision in dynamics. Chemoprophylaxis HIV infection at pregnant women descend frequency transmission HIV to newborn with 50% to 5%. Realization hemostatic caesarean section permit descend frequency transmission HIV to newborn with 10% to 2%. Thus, the creation of women dispensary system and organisation of newborn help and the choice of optimum obstetrics tactics with the virus-bacterial infections pregnant women are the necessary condition for the decrease of perinatal mortality and morbidity.

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How do HIV-positive women conceive?

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Background: Many HIV-positive women want to have children. During pregnancy most of these women are cared for by an interdisciplinary team. However, in many cases the method of conception remains unclear, especially in serodiscordant couples or women with a partner whose HIV-status is unknown.

Methods: All HIV-positive pregnant women (n=121) seen at the Department of Obstetrics (Charité Virchow-Klinikum, Berlin) between January 2007 and February 2009 were prospectively interviewed about the HIV-status of their partners and method of conception.

Results: The HIV-infection was diagnosed in the index pregnancy in 35 women (28.9%). 57.4% of the women who knew about their infection before pregnancy came from sub-Saharan Africa, 22.3% from Germany, and 10.2% from Eastern Europe. 39 of these women (45.3%) already had one or more children. 16 women (18.6%) became pregnant by self-insemination, 5 (5.8%) by IVF or intrauterine insemination (IUI). 8 women had unprotected intercourse with an HIV-positive partner. Further 45 women (52.3%) had unprotected intercourse with an HIV-negative partner or one whose HIV-status was unknown. A large proportion (61.5%) of the 65 planned pregnancies resulted from unprotected intercourse. Other methods of conception were only very rarely used by immigrant women (5/50).

Comment: A high percentage of positive women reports having had unprotected intercourse with a partner with negative or unknown HIV-status in order to conceive. Better and earlier counseling about methods of conception as well as family planning are clearly necessary.

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HIV-HCV co-infection in pregnancy: Rate of vertical HCV transmission after caesarean section

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Background: Maternal co-infection with human immunodeficiency virus (HIV) has been implicated as an important co-factor for enhanced vertical transmission of hepatitis C virus (HCV).

Methods: We evaluated the rate of mother-to-child transmission of HCV in women with HIV/HCV co-infection who delivered via caesarean section at Charite Virchow Hospital between 1998 and 2008. Additionally, data concerning virus load, maternal age and history of intravenous drug abuse was analyzed. Results: So far, 35 HIV/HCV co-infected patients have been evaluated. 77.1% (27/35) of the women had a history of intravenous drug abuse and were substituted or used drugs during the index pregnancy, their mean age was 29 years. The follow-up time for 34 of the 35 children was more than 12 months. All children showed a negative HCV-antibody status, and HCV-PCR was negative in all children.

Discussion: Preliminary data show no case of vertical HCV-transmission in the analyzed group of 35 pregnancies. In published meta-analyses the rate of mother-to-child transmission ranges from 4 to 10%; viremic women are more likely to transmit HCV with reported transmission rates up to 80%. The discussion about the influence of the mode of delivery on HCV transmission rate is controversial. Our data suggests that a caesarean section as delivery mode can help to lower the risk of vertical transmission of HCV.

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HIV-infected pregnant women – impact of mode of delivery

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Introduction: Perinatal rate of HIV transmission has declined over the years as a result of a group of measures known to reduce this transmission. Our aim is to analyze the impact of mode of delivery in vertical transmission in our population.

Material and Methods: Retrospective review of medical files of HIV-infected pregnant women and their newborns delivered in a tertiary referral centre between January/2001 and December/2007 and analysis of mode of delivery and perinatal transmission.

Results: 51 HIV-infected pregnant women delivered in our Institution. 9 women (17.6%) did not attend medical care and their HIV status was only identified during or after labor. Of those women diagnosed before or during pregnancy, 37 were on HAART, 3 were on AZT and 2 women did not follow medical prescription. HAART was done in 73%. Preterm birth occurred in 6 cases. Vaginal delivery was encouraged in those with no contraindications - 11 women accepted this mode of delivery; 8 women delivered vaginally. The resulting 42 pregnant women delivered 43 newborns. HIV infection was diagnosed in 1 child – delivered by cesarian section. Transmission rate was 2.3%. All women but 2, delivering by cesarian section, had uncomplicated puerperium. There were no maternal complications occurring after a vaginal delivery.

Conclusion: We found that vaginal delivery in women who fulfilled clinical criteria was not associated with any case of vertical transmission. Encouraging vaginal delivery in motivated pregnant women, with no contraindications, results in optimal outcomes with minimal maternal and neonatal complications.

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Vertical transmission of HIV infection in the era of HAART

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Objectives: To assess risk of HIV vertical transmission (VT) in the era of highly active antiretroviral therapy (HAART).

Methods: A prospective cohort of 264 HIV-infected pregnant women who delivered in a University Hospital in a 10 years period (1999-2008) was assessed. All pregnant women were tested for HIV in the first visit and those with risk factors were retested in the third trimester. An emergency HIV test was performed when no Result was available at delivery. Pregnant women were treated in accordance with current Spanish Perinatal guidelines for the prevention of HIV VT.

Results: All the 256 live newborns born during the study period were tested for HIV. A single case of vertical transmission was identified (0.39%), from a woman who tested negative 6 weeks before delivery. She was an active non-intravenous drug user (IVDU). Her long term male partner was an active IVDU and was HIV-HCV co-infected with no current medical follow-up or HAART. The pregnancy was planned without medical preconceptional counseling. A precipitated preterm delivery occurred at 35.6 weeks of pregnancy and the women tested HIV positive 48 hours after delivery. No VT prevention measures were applied peripartum either in the mother or the newborn.

Conclusions: Vertical transmission of HIV is exceptional with current preventive measures. A primary HIV-infection can occur during pregnancy and should be diagnosed to avoid VT. Intrapartum rapid HIV-test should be performed not only in women without a previous screening Result but also in those with known risk factors, to apply prevention measures if necessary.

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Preventing symptomatic fetal cytomegalovirus infection by off-label hyperimmune globulin-prophylaxis during pregnancy – a German and Swiss perspective

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Background: Primary maternal cytomegalovirus (CMV) infection is the major risk factor for symptomatic congenital infection as maternal immunity reduces the risk of transmission to the fetus.

Objective: To assess both the clinical benefit as well as the administrative difficulties of off-label CMV maternal hyperimmune globulin-prophylaxis (HIG) in patients with primary CMV seroconversion during pregnancy.

Patients and Methods: We examined 30 women and their newborns, who were treated with hyperimmune globulin-prophylaxis after primary maternal cytomegalovirus (CMV) infection during their course of pregnancy. No fetus, with or without CMV-associated ultrasound abnormalities, was excluded. Fetal sonograms were evaluated before and after HIG infusions.

Results: Cytomegalovirus virus is transmitted to the placenta and fetus causing congenital infection despite maternal hyperimmune globulin-prophylaxis (HIG) in some cases. However none of these infants born had signs or sequelae of symptomatic CMV infection. The HIG-therapy was well tolerated by the mothers and children. No side-effects of HIG-treatment occurred.

Conclusion: The outcomes of the infants born to HIG-treated mothers support the efficacy of HIG as a possible treatment to reduce the risk of congenital symptomatic CMV infection. CMV hyperimmune globulin may be of value against the consequences of transplacentally transmitted CMV.

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Diverse outcome after neonatal listeriosis: A case series

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Objective: Perinatal listeriosis is associated with an increased risk of stillbirth and neonatal death. Clinical manifestations and outcomes of listerial sepsis in the neonate are highly variable, as described in the present study.

Study Design: Retrospective analysis of all neonates with proven or suspected listerial infection treated in a level three university hospital from 2000 to 2009.

Result: A total of 10 cases with proven or suspected neonatal listeriosis were studied. Median gestational age and birth weight were 30.5 weeks (range 26.9-41.1 weeks) and 1,525g (range 820-4,240g), respectively. All patients with microbiologically proven listeriosis (8/10) manifested symptoms on the first day of life, whereas two infants with confirmed maternal infection but negative cultures were clinically unremarkable. Symptoms were unspecific and included poor condition, arterial hypotension, and respiratory insufficiency. Laboratory Results showed elevated C reactive protein, interleukin-6 and, invariably, a marked white blood cell left shift. None of the patients developed meningoencephalitis as evidenced by typical cranial ultrasound or CSF findings. One infant had bilateral grade 3 intraventricular hemorrhage on day 1. Antibiotic therapy was initiated with ampicillin+gentamycin (4/10) or with cefotaxim+piperacillin and converted to ampicillin±gentamycin in case of positive culture Results. One infant died after unsuccessful resuscitation immediately following birth. All other patients survived without sequelae.

Conclusion: Neonatal listeriosis is a potentially fatal infection. However, when antibiotic treatment is administered in a timely manner, central nervous system involvement can be avoided, and the prognosis is favorable.

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Epidemiology, perinatal infection risk and neonatal discharge outcome of substance use in pregnancy – a 5 year experience

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Introduction: Substance use in pregnancy poses neonatal risks related to maternal lifestyle, drug use, perinatal infection and child protection issues. This study aims to evaluate these predisposing factors.

Methods: Pregnant women with history of substance use were identified from ‘cause for concern’ referrals at our hospital between January 2003 and December 2007. Data was collected retrospectively on mother-infant pairs from medical and laboratory records and analyzed on Excel 2003.

Results: 168 women were identified with history of substance use in pregnancy. 90% were unmarried, 42.3% single and 85.4% unemployed with median age of 25 years. 97.4% smoked and 61.3% were polydrug users. Methadone, heroin and cannabis were the most frequently used drugs. Infection screen for HIV, Hepatitis B & C were undertaken in 85%, 82% and 58% women respectively. 30% of those screened were positive for Hepatitis C, 5% for Hepatitis B, 17% for chlamydia and none for HIV or Syphilis. Babies of seropositive mothers were twice more likely to complete Hepatitis B vaccination schedule (71% vs. 35%). Hepatitis C PCR was negative in all babies with available Results. 21% newborns were on the Child Protection Register, 17.7% placed in foster care and 14.3% breastfed at discharge.

Conclusions: Smoking, unemployment and single status were frequent with substance use. Hepatitis C prevalence was high with scope for improving screening rates. Hepatitis B immunization should be targeted to at-risk infants of seropositive mothers. Understanding the socio-clinical risk profile may help direct healthcare resources appropriately.

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Endotoxin (LPS) affects fetoplacental barrier in dually perfused term human placentas

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Objectives: Intrauterine infection lead to increased perinatal mortality and morbidity. Clinical studies have shown an 11-fold increased risk for neurological disturbances after antenatal bacterial infection. Using dual perfusion of the term human placenta we studied the effects of endotoxin (LPS = lipopolysaccharides) on villous trophoblast and fetal vessels.

Methods: After C-section normal term placentas were dually perfused for 6 h using medium with and without 100 µg or 500 µg LPS/l medium; LPS-treated and non-treated placental cotyledons were paraffin embedded, sections were performed and stained for E-selectin, ICAM-1 and cytokeratin 18 by immunohistochemistry, and semiquantitative morphometry was performed for evaluation; t-test was used for statistical analysis (s: p<0.05).

Results: LPS in the fetal circulation led to a significant increase in the expression of E-selectin (p =0.007) and ICAM-1 (p =0.03) from the fetal endothelium, independent of the LPS concentrations used. LPS in the intervillous space led to a similar upregulation of E-selectin and ICAM-1 in the syncytiotrophoblast and a significant reduction of cytokeratin 18 expression (p<0.03).

Conclusion: Circulation of endotoxin in the placenta may cause activation of the fetoplacental endothelium and/or syncytiotrophoblast and shows a negative effect on the trophoblast cytoskeleton. Activation and alterations of the feto-placental barrier may disturb placental function subsequently leading to intrauterine fetal growth restriction.

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Reduced concentration of circulating progenitor cells in patients with preeclampsia during and after pregnancy

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Introduction: Circulating progenitor cells (CPCs) and endothelial progenitor cells (EPCs) are essential for vascular repairing processes. A reduction of their concentration is associated with an increased cardiovascular risk. Thus they might play an important role in the pathophysiological pathway of hypertensive pregnancy disorders and their generally increased cardiovascular risk after pregnancy. The aim of this study was to analyze the dynamic of CPCs/EPCs in normal and preeclamptic pregnancies.

Methods: In this prospective study, 20 preeclamptic and 22 normal pregnancies were included and matched by gestational age. CPCs/EPCs were analyzed at inclusion and within the first postpartal week. CPCs were quantified by FACS as CD3-/CD34+ circulating mononuclear cells. EPCs were characterized 7 days after isolation of mononuclear cells by the Ficoll-gradient through the uptake of acetylated LDL and the binding of lectin.

Results: In preeclamptic pregnancies, CPC were significantly reduced compared to controls (149±27 vs. 284±42 perml, p<0.01). EPCs however did not differ in both groups (90,932.6±17,995 vs. 93,536.0±12,649 per 5x10⁶ mononuclear cells). During the first postpartal week the reduction of CPCs was still measurable (173.3±28 vs. 287.2±58 perml, p<0.07).

Conclusion: The concentration of CPCs is significantly reduced during preeclamptic pregnancies. The demonstrated alteration in the dynamic of these cells does not normalize immediately after birth. An on-going study will show if the reduced quantity of CPCs in preeclamptic women can still be shown 6 months after the end of pregnancy.

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Systemic lupus erythematosus and pregnancy – a retrospective study

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Introduction: Systemic lupus erythematosus (SLE) is a disease predominantly affecting women in their reproductive years. Pregnancy is associated with exacerbations of SLE, and there is a higher incidence of adverse maternal and perinatal outcomes.

Objective: The purpose of this study was to evaluate maternal and perinatal outcomes of pregnancies complicated with SLE.

Material and Methods: Retrospective study of all pregnant women with SLE surveilled at our department from January 2004 to December 2007. Significant maternal, fetal and neonatal complications were registered.

Results: Data from 29 pregnancies (26 patients) complicated with SLE were reviewed. Mean maternal age was 30.9 years, and mean duration of disease was six years. Sixty-six percent had cutaneous and joint manifestations. Antiphospholipid syndrome was present in 28% of patients, and 24% had autoantibodies anti-SSA or anti-SSB. Thirteen patients (44.8%) required treatment with glucocorticoids, 9 (31.0%) with hydroxychloroquine and 4 (13.8%) with azathioprine. Concerning exacerbations of the disease there were 5 (17%) cases of mild to moderate flares and 6 (20%) of severe flares (the majority being renal flares – 13.7%). Ten percent of pregnancies were complicated by preeclampsia. There were 5 (17%) spontaneous abortions in the 1st trimester, one (3.5%) fetal death, 2 (7%) fetal growth restrictions, 5 (17%) preterm births and 2 (7%) Neonatal Intensive Care Unit admissions.

Discussion: Due to increased maternal, fetal and neonatal risk, pregnant women with SLE should be carefully surveilled by a multidisciplinary team and with differentiated perinatal support.

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Retrospective study on the courses of 26 pregnant women with immune thrombocytopenia

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Maternal autoimmune thrombocytopenia (ITP) in pregnancy is a rare disease (incidence of 1:1000) that affects mother and child. It is still controversial whether treatment of the thrombocytopenic mother by corticosteroids or intravenous immune globulines (IVIG) can prevent antiplatelet IgG antibodies from crossing the placenta as well as if elective caesarean section can prevent intracranial hemorrhage in the thrombocytopenic newborn. So it was the aim of this retrospective study to review the course of pregnancies of pregnant women with ITP during a 10-year period.

Material and Methods: The cases of all pregnant women that were treated for ITP at our department were reviewed with special regard to treatment during pregnancy, mode of delivery and neonatal thrombocytopenia.

Results: Twenty-six pregnant women were identified with the diagnosis of ITP. Eleven of them received cortisone therapy during pregnancy, 15 IVIG and 9 patients received both, 8 patients had no treatment. Fifteen women underwent elective caesarean section, 5 women had emergency caesarean and only 6 women vaginal delivery. Thrombocytopenia was diagnosed in 7 newborns with 6 newborns requiring platelet transfusion. There was no case of intracranial hemorrhage. Neonatal thrombocytopenia occurred despite of maternal treatment during pregnancy and did not correlate to maternal platelet counts before delivery.

Conclusion: Neonatal thrombocytopenia can occur in pregnant women even with normal platelet levels or immunosuppressive treatment. So, the role and indication of a preventive caesarean section remains in discussion.

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Automated measurement of sFlt-1/PIGF-ratio allows precise determination of preeclampsia

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Objective: The angiogenic factors sFlt-1 and PIGF are closely involved in the pathophysiology of preeclampsia (PE) and suggested to be important diagnostic markers for the disease. The objective is to evaluate newly developed automated assays for sFlt-1 and PIGF (Elecsys sFlt-1 and Elecsys PIGF), to establish gestational age dependent reference ranges, and to test the sFlt-1/PIGF-ratio (preeclampsia anti-angiogenesis index, PAAI) as an aid in diagnosis for PE.

Study Design: This multicenter case-control-study includes 351 patients, 71 patients with manifest PE and 280 gestational age matched controls from five European study centers. A total of 595 serum samples were collected and sFlt-1 and PIGF levels were measured. For each serum-sample the PAAI was calculated and preliminary cut-off values for clinical use regarding diagnosis of PE were established.

Results: Automated measurement of sFlt-1 and PIGF significantly discriminates between healthy and diseased patients throughout pregnancy. The PAAI proved to be an excellent discriminator between PE and controls with an AUC of 95%. Highest accuracy was reached in the subgroup “early onset preeclampsia” with an AUC of 97%.

Conclusions: The Elecsys assays for sFlt-1 and PIGF allow automated measurement and fast assessment of the PE-status of a patient in the clinical context. The PAAI proved to be an accurate aid in diagnosis of PE. It is suggested to implement the PAAI in the diagnostic algorithm of PE. Prospective studies are needed to evaluate the role of PAAI as an aid in prediction.

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Neonatal morbidity following substance use in pregnancy – a 5 year experience

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Introduction: There are significant medical and social morbidities in newborns related to substance use in pregnancy. The socio-clinical profile of this population is changing and contemporary published data is limited.

Methods: Pregnant women with history of substance use were identified from ‘cause for concern’ referrals at our hospital between January 2003 and December 2007. Data was collected retrospectively on mother-infant pairs from medical and laboratory records and analyzed on Excel 2003. Nonparametric data was analyzed using Mann Whitney U test.

Results: 168 (0.94%) of 17816 live births were born to women with history of substance use in pregnancy. 22.8% of infants were preterm and 28.5% small for gestation. 59 babies (35.1%) required admission to neonatal unit of which 26 (15.5%) required pharmacological treatment for withdrawal symptoms. 95% babies showed peak withdrawal symptoms within 5 days. No death was reported. Other morbidities were related to complications of prematurity, low birth weight (LBW), hypoglycaemia and need for sepsis screen.

The median duration of hospital stay reduced from 12 days in 2003-2006 to 7 days in 2007 following change in guidelines without rise in readmission rate (p<0.001).

82.3% babies went home with their mother but only 14.3% breastfed at discharge. 21% of infants were placed on the child protection register.

Conclusions: Neonatal morbidity remains high with substance use in pregnancy, principally related to complications of prematurity, LBW and treatment of withdrawal symptoms. Prolonged hospital stay can be reduced safely and may have significant impact on resource allocation.

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Breastfeeding in women with benign breast disease

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Objective: Benign breast disease (BBD) is very common among women in their fertile age, but its etiology and effects on the reproductive function remain unclear. Our study aims to investigate the eventual influence of BBD on breastfeeding.

Materials and methods: We collected data about 105 women with BBD, focusing on the reproductive history and breastfeeding. We analyzed data by R (version 2.8.0) considering significant p<0.05.

Results: Fibroadenoma represents the most cases of BBD 55% (58/105), followed by fibrocystic mastopathy 19% (20/105), mastodynia 11% (11/105), ductal ectasia 6% (6/105) and mastitis 5% (5/105). Mean women age is 31.55 years (± 6.15), BMI 21.23 kg/mq (± 3.39) and age at menarche 12.96 years (± 1.53). 60% (63/105) of women have ever used contraception, 35% (37/105) have ever become pregnant and 92% (34/37) of them breastfeeded with a mean duration of 14.78 months (± 13.08). By monovariate analysis, there seems to be no significant difference between nullipara and the other women divided in 2 groups based on breastfeeding duration, considering as cut off both the 3rd quartile of cumulative breastfeeding (20 months) or the 3rd quartile of breastfeeding per child (13 months). Only chronological and gynecological age Result significantly different (p<0.05), but probably because of their direct correlation with parity. Among women who breastfeeded, by monovariate linear regression considering only fibroadenoma, there is a direct correlation between breastfeeding duration and number of benign lesions (p<0.05), which remains significant also by multivariate analysis.

Conclusions: There seems not to be any influence of BBD on breastfeeding, which is probably more influenced by other factors, such as overweight and personal choice.

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Acute myeloblastic leukaemia in pregnancy – report of 4 cases

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Background: Acute myeloblastic leukaemia (AML) has an estimated overall incidence of 3 per 100 000 pregnant women. Thus, AML in pregnancy is extremely rare. In most cases immediate treatment is required. Optimal timing of hematologic and obstetric management is needed to avoid serious complications.

Cases: Four cases of AML in pregnancy diagnosed at different weeks of gestation are reported. Two women received induction chemotherapy in pregnancy. One of them had an elective caesarean delivery in 30/6 weeks of gestation. The other one suffered a stillbirth. The remaining two received therapy only after termination of pregnancy – a spontaneous delivery at term and an induced abortion in 14 weeks of gestation. Two patients received allogeneic stem cell transplantation after consolidation therapy. In all cases follow-up data (18 to 60 months) of mother and child are reported.

Comment: Successful treatment requires an optimal timing of hematologic and obstetrical management by predicting and monitoring maternal and fetal parameters using ultrasound and serial Doppler recordings. Individual therapy-related side effects have to be anticipated in mother and child.

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Renal transplantation and pregnancy: What outcome?

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Background: Pregnancy after renal transplantation increases risk of maternal and fetal complications when it occurs in the first year from transplantation.

Objective: To evaluate the outcome of pregnancies in renal transplant recipients referred to our centre.

Methods: Retrospective study of 12 pregnancies in 12 renal recipients followed in a single tertiary Centre from January 2002 to February 2009.

Results: Mean maternal age at pregnancy was 28±5 years (range,20-35) and the interval between transplant and pregnancy varied between 1 and 100 months (53.7±30.27 months). All women were submitted to immunosuppression during the entire pregnancy, (6 with tacrolimus and 6 with cyclosporine). The fetal outcome included 11 live births (91.6%), 1 stillbirth (8.4%). The most frequent maternal complications were hypertension in 8 pregnancies (66.6%), 1 (12.5%) of which ended in pre-eclampsia; urinary tract infections in 3 (25%) pregnancies; one case of gestational diabetes mellitus (8.3%), one of anemia (8.3%); one case (8.3%) of oligohydramnios and one of anhydramnios (8.3%). Median creatinine level was 1.0 (range, 0.4-2.8)mg/dl before conception and 1.2 (range, 0.8-1.3)mg/dl after delivery. The major fetal complications observed consisted of 7 (58.3%) IUGR. In all cases, a caesarean section was performed. Of the 11 successful pregnancies, 6 (54.4%) resulted in term deliveries and 5 (45.6%) in preterm deliveries (range, 34.1-36 weeks). The mean birth weight of the offspring was 2042.5g (range, 1730-2600g).

Conclusions: Risks of obstetric and perinatal complications seem to be increased. Further studies of long term graft function and pediatric follow-up are needed.

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Multiple sclerosis and pregnancy: A study of 59 cases

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Objective: To study the effects of pregnancy in the course of multiple sclerosis (ME) and obstetrics and perinatal associated complications. To analyze the becoming factors of the attacks.

Methods: Retrospective descriptive study of 59 pregnant women with ME at our hospital from 1995 to 2008. It was done a logistic regression (forward-LR method) between the following variables: age, number of previous pregnancies and deliveries, previous surgeries, woman age at beginning of the disease and years of evolution, complications during pregnancy and previous treatments. Results: Mean age of the patients was 33 and the mean of years of evolution 6.72±3.95. 48 healthy children were born (81.4%) and there were 11 abortion (18.64%). Only 8.5% of pregnancies were preterm. 67.8% of newborn child had a right weight and only a 10.2% of them was underweight. Cesarean section rate and instrumental delivery rate was 19.14% and 36.84% respectively. The vaginal spontaneous delivery was the most frequent route of delivery (80.85%). 5 patients (10.64%) had some attacks during the pregnancy. Exasperations of the disease were not described in three postpartum months, despite the lack of treatment (only 23 patients had taken prophylactic treatment after delivery. No becoming factors of ME attacks had been found when the logistic regression was done.

Conclusions: According to our Results, the pregnancy in women affected by ME can not be discourage. The vaginal spontaneous delivery may be the elective route of delivery. The rate of attacks during the pregnancy is low, and no related factors had been found about this.

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The psychological status and anxiety in normal and high risk pregnancies

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Objective: This study was conducted with the aim of determining the level of anxiety and problems experienced by pregnant women in their last trimester who came to the prenatal clinic for check-up and pregnant women who are hospitalized because of a risk factor related to pregnancy.

Method: The research was conducted as a descriptive and comparative study. 100 women having a high risk pregnancy and 100 women experiencing a healthy pregnancy participated in the research. Women’s anxiety was measured using Spielberger’s State and Trait Anxiety Inventory.

Results: In this study both the healthy (X=50.59) and the at-risk pregnant women (X=50.43) had trait anxiety score means clearly higher than normal. In addition, although not as high as the trait anxiety score means, both the at-risk (X=42.17) and the healthy pregnant women (X=43.17) had higher than normal state anxiety score means. The hospitalized pregnant women’s highest rate of anxiety was that their current risk factor would hurt their infant and were bothered by and worried of being hospitalized. Furthermore, increase in the period of hospitalization as well as living in rural areas as compared to urban areas were found to be factors leading to higher anxiety.

Conclusions: Nurses and midwives need to exert more effort in recognizing the emotional problems experienced by women and their families during pregnancy to ensure that holistic care is provided which will support pregnant women emotionally and psychologically to decrease the negative effects caused by stress.

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Continuous FHR scoring-procedures: A new approach

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Background: Hypoxia and acidosis influence both the fetal heart-rate (FHR) and all acid-base variables of the fetus. We aimed at a clinically valid pH-prognosis by electronic evaluation of FHR-patterns.

Methods: The FHR-signal during the last 30 min. of delivery of 471 fetuses was stored and further processed electronically (MATLAB). Oscillation amplitude (OA), microfluctuation (MICRO) and the mean frequency (FRQ) were computed for every min. After adjustment of each parameter according to empirical weighting a new index was designed:

\[ \text{WAS-index} = \frac{\text{MICRO} \times \text{FRQ}}{\text{OA}} \]

The mean of 30 subsequent WAS-indices was named WAS-score. This score was correlated (r, Rho) with pH, BEoxy., pCO2 and sO2 measured (RADIOMETER) in umbilical artery blood immediately after birth. Using linear regression analysis each WAS-score was used for pH-determination. Moreover the WAS-index (computed for one min.) could be determined every second which leads to 60 pH-values / min. (using again regression analysis) which now serve for continuous control of fetal well-being.

Results: Correlation-analysis of the WAS-score with pH, BEoxy., pCO2 and sO2 leads to the following coefficients: \( r = 0.644, 0.570, -0.500 \) and 0.254 respectively. \( P \) all \(< 0.0001\). The behavior of the index is demonstrated by video in two fetuses with terminal acidosis. The adjustment procedures are demonstrated as well.

Conclusions: Fetal acidaemia can be predicted with the WAS-score in clinically reasonable limits using only OA, MICRO and FRQ after adequate adjustment of each variable. Computation of the WAS-index every sec. Thus leads to continuous control of fetal well-being which seems to be quite similar to a continuous pH-evaluation. The original CTG remains untouched.

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Spectral power of fetal heart rate variability can be used to predict fetal scalp blood pH

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Introduction: Spectral analysis of fetal heart rate variability is related to fetal condition. Previous studies found that an increased normalized low frequency (LFn) power is associated with fetal acidosis. In addition to fetal monitoring by cardiotocogram, fetal scalp blood sampling and STAN® are used to reduce the number of unnecessary interventions for presumed fetal distress. The objective was to study if normalized low frequency spectral power can predict fetal scalp blood pH.

Methods: Ten-minute continuous STAN® segments, preceding the scalp blood measurement, were used to determine fetal beat-to-beat heart rate. Spectral analysis was performed using a Fourier transform. Spectral power in the low frequency band (0.04-0.15Hz) was calculated. In addition, normalized values were determined by dividing low frequency power by total power (0.04-1.5Hz). Fetal scalp blood pH values were predicted from LFn power. Some of the women included underwent more than one fetal scalp blood sample. Therefore, linear regression models were estimated on the basis of the method of generalized estimating equations.

Results: In total 39 fetal blood samples from 30 patients were studied. We found that LFn power could significantly predict fetal scalp blood pH. The estimated $\beta$ of LFn was -0.4 (95% confidence interval (CI) -0.7 to -0.1) and the odds ratio was 0.69 (95% CI 0.51-0.94).

Conclusion: LFn power can significantly predict fetal scalp blood pH. Spectral values might be incorporated into STAN® to decrease false negative Results. However, prospective studies should be performed in advance.

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The use of PR interval - fetal heart rate correlation analysis in intrapartum fetal monitoring: A systematic review of the literature

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Background: Since the introduction of continuous electronic monitoring has not benefited neonatal outcome and led to increased intervention rates, new methods for fetal surveillance have been investigated. Research into fetal electrocardiogram waveform changes has focused on morphologic features (T/QRS complex) and time interval (PR interval) changes. Time interval changes are robust measurements thought to be especially useful when the fetal electrocardiogram is obtained from electrodes on the maternal abdomen. We aimed to assess the diagnostic properties of the PR interval – fetal heart rate correlation analysis.

Methods: A systematic search was performed in the electronic databases CENTRAL (Cochrane Library), EMBASE and MEDLINE up to March 2009. Articles that described PR interval – fetal heart rate correlation analysis and compared conduction index or ratio index with any measure of fetal outcome, such as umbilical blood-gas values, were included.

Results: Six studies met the inclusion criteria, assessing the outcome of 2413 fetuses. In 2202 cases sufficient data was obtained for analysis. The Results of included studies will be pooled to define diagnostic properties of the test.

Discussion: While the Results of four observational trials and one randomized controlled trial were promising, a large multi-centre randomized controlled trial did not show a significant benefit from using PR-interval – fetal heart rate correlation analysis. There are indications this could be due to non-adherence to the protocol.

Conclusion: The Results of studies regarding the use of PR interval – fetal heart rate correlation analysis in conjunction with cardiotocography in fetal monitoring are inconclusive.

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Complex fetal assessment during labor

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The common cause of fetal morbidity and mortality is perinatal asphyxia – medical, ethical and forensic problem. We evaluated correlations and validity of different methods and their combinations for fetal distress diagnosis.

Simultaneous continuous intrapartum monitoring with cardiotocography (CTG), fetal pulse oxymetry (FPO) and the analysis of ST segment of fetal ECG (STAN) was performed in 67 term deliveries. Fetal metabolic status was verified by examination of acid-base parameters, umbilical concentrations of lactate, erythropoietin (EPO), and protein S100B. The criterion for metabolic acidosis (MAC) was pH<7.15, resp. BD>12mmol/l.

Significant differences have been found among non-acidotic (n=36) and acidotic (n=31) fetuses in the CTG, FPO, acid-base parameters, and lactate and EPO concentrations. The most valid biophysical approach in fetal distress diagnosis was combination of simultaneous continuous monitoring with CTG, FPO and STAN (Spearman test: p<0.05, Kendall test: p<0.0005). Effective monitoring time decreased subsequently: CTG–STAN–FPO. Our Results confirmed an excellent correlation between acid-base parameters, lactate and EPO levels. The best validity for MAC prediction had lactate concentration. The highest sensitivity had lactate and EPO concentrations, and the highest specificity had simultaneous continuous monitoring (CTG, FPO and STAN) and lactate levels.

The most objective diagnostic approach of fetal distress is a simultaneous continuous monitoring with CTG, FPO and STAN with complex postpartum verification of fetal metabolic status with acid-base parameters, umbilical lactate, and EPO levels.

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External FHR-monitoring: Do we really trace the fetus?

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Introduction: Signal ambiguity can Result in unexpected outcome with external fetal heart rate (FHR) monitoring (1). This is due to difficulties to differentiate between fetal and maternal heart rate signals visually and by the autocorrelation technique. Therefore the question arises whether external FHR monitoring systems always trace the fetus reliably.

Patients and Methods: In 7 patients, both maternal and fetal heart rate were simultaneously traced on separate tracks during labor and delivery. External FHF monitoring systems for twins were used, with the FHR on the first, and the maternal heart rate on the second track. Occasionally the FHR was traced directly by an internal fetal scalp electrode.

Results: In only 2 patients fetal and maternal heart rate could be clearly differentiated visually over the complete monitoring period. The other 5 patients showed repetitive periods during which maternal and fetal heart rate interfered with each other. In one case a pattern of repetitive FHR decelerations appeared simultaneously with maternal accelerations. Without the double tracing in this case the maternal accelerations might have been misinterpreted as fetal well-being leading to a seemingly unexplainable adverse fetal outcome.

Conclusion: Our study shows that it might often be necessary to either use direct internal FHR registration or double tracing of maternal and fetal heart rate signals in order to identify the fetus clearly at any time during labor and delivery. Visual identification of external FHR patterns, generated by the autocorrelation technique, may be misleading.

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Does access to computerized cardiotocogram analysis affect the clinical prediction of newborn umbilical pH and Apgar scores?

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Objective: To evaluate whether access to computerized CTG (cCTG) analysis affects clinicians’ reproducibility and validity in prediction of newborn umbilical artery blood pH (UAB) and Apgar scores (As).

Methods: Intrapartum CTG tracings of singleton term-pregnancies monitored internally until a maximum of 5 or 20 minutes before vaginal or caesarean delivery, respectively (n=204) were randomly assigned to computer analysis by Omniview-SisPorto 3.5® (n=104) or no analysis (n=100). Three obstetricians were asked to evaluate tracings independently and to predict the newborn’s UAB and As. Inter-observer agreement and precision on prediction of these values were assessed using the Intraclass Correlation Coefficient (ICC), percentage of correct predictions within 0.10 of real pH values and a margin of 1 for As, and the Limits of Agreement (LA), all with 95% confidence intervals (95%CI).

Results: Interobserver agreement on UAB estimation was significantly higher in the cCTG group ([ICC=0.70 (95%CI=0.61-0.77] versus ICC=0.43 (95%CI=0.21-0.60)), and this group also showed non-significant trends towards higher agreement on estimation of 1 and 5-minute As. In the cCTG group observers predicted UAB correctly in 70% of cases (95%CI=0.61-0.79), while in the control group this occurred in 46% (95%CI=0.35-0.56). LA for observer-outcome agreement in UAB estimation were -0.16; +0.11 in the cCTG arm and -0.21; +0.14 in the control group. Non-significant trends were seen towards a better prediction of As with access to cCTG.

Conclusions: Access to computerised analysis of CTGs significantly improves interobserver agreement between clinicians and their precision in prediction of newborn UAB.

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Maternal body-mass-index has a relevant impact on the signal quality of fetal heart rate traces and on academia at birth

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Objective: Is there a relation between maternal weight (BMI kg/m2), the signal processing of the fetal heart rate monitor, the quality of the displayed fetal heart rate traces and the acidemia after birth?

Methods: In a prospective randomized observational study 354 deliveries very surveilled with the most recent fetal heart rate monitors from HME (Sonicaid FM 800) und Philips (Avalon FM 30+50). During the study Philips developed a new algorithm which was applied in 101 deliveries while the classic software was used in 136 cases. The HME technology was applied to 117 fetuses. The three groups did not differ concerning maternal age, parity, BMI in early pregnancy and at term. Each heart rate trace was analyzed in steps of one second in the last hour of stage I and the last 30’ of stage II.

Results: The time of signal loss increased with BMI. In stage I the median time without detected fetal heart rate rose from 2' and 20'' (BMI<30) to 4' (BMI>30) and in stage II from 3'30'' (BMI<30) to 4'30'' (BMI>30). Acidemia in the umbilical artery after birth was more often with overweight (BMI<30.0: 19.5%, BMI<30.0: 26.5%), p =0.046. The rate fetal scalp blood samples during delivery rose with maternal overweight.

Conclusion: The most recent fetal monitoring technology provides an almost 95% exploitation of reliable heart rate signals. However maternal overweight is a relevant risk for fetal surveillance and leads to increased academia.

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Homemonitoring of high risk pregnancies by midwives of the Academic Medical Centre, Amsterdam

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During the nineties of last century in the Academic Medical Centre in Amsterdam a successful investigation runs, entitled: “Fetal monitoring at home in high-risk pregnancy”, an integrated clinical and economic evaluation. The study shows no contraindications for the implementation of domiciliary maternal and fetal monitoring. It shows that obstetrical and neonatal outcomes were not affected as ante-natal monitoring in the hospital would be replaced by monitoring at home. This homemonitoring (HM) is just as safe as monitoring in the hospital. Included for HM are still women with high risk pregnancies, indicated for daily fetal and maternal surveillance, who have restricted mobility. Suitable portable equipment for fetal surveillance at home, even as capable professionals, the secondary care midwives of the AMC, stand for quality and continuity of care. This hospital care at home requires strict protocols for patient and caregiver concerning ability, responsibility and communication skills. Important patient conditions are the distance to hospital and an appropriate daily care by family and friends in a suitable home. The daily surveillance include: CTG, blood pressure, blood research, urine tests and observation of the patient. HM is a challenge for professionals to work outside the hospital with other responsibilities. Autonomy and a more in balance family life are huge advantages for women. At present 20 hospitals in The Netherlands are offering HM to their patients.

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Objective and non-invasive detection of fetal movement

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Reduced fetal motility is associated with fetal death. Since maternal perception is liable to significant inter-patient variability, clinical actions based on fetal movement counting by the mother do not necessarily improve fetal outcome. If it were possible to assess fetal movement in an objective way, however, this would resolve issues on maternal impartiality and hence could become of significant value in supporting cardiotocography for ante partum fetal monitoring.

Building on a method to extract the fetal electrocardiogram (fECG) from electrophysiological recordings on the maternal abdomen, we conceived a method for non-invasive and objective monitoring of fetal movement. By describing the spatial fECG unambiguously through the fetal vectorcardiogram (fVCG), variations in the fECG are related to movement of the fetal thorax. Moreover, visualization of the evolution of the fVCG over time provides a direct indication of fetal movement and has been validated by comparing it to simultaneously performed ultrasound analysis. This comparison suggests that automated analysis of the fVCG across successive heartbeats should permit physicians to monitor fetal movements quantitatively and objectively for long periods of time, thus providing vital information on fetal motility and sleep/activity patterns. Moreover, as the method does not expose the fetus to ultrasound, it can be applied 24 hours per day.

This approach may pave the way to a non-invasive, automated, reliable, and objective method to monitor fetal movements during all states of pregnancy, 24 hours per day. With future research it might be supplemented with fECG analysis, further enhancing its diagnostic value.

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The relationship between maternal birth positions and maternal and neonatal outcomes in a birth centre over 12 years

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Whilst there is evidence that upright birth positions provide advantages, for women compared to supine birth positions (Gupta & Hofmeyer, 2006), there is limited evidence about differences in outcomes between individual upright positions. This paper reports on research examining the relationship between different maternal birth position and perineal trauma in a birth centre attended by low risk women having normal vaginal births in Sydney over 12 years.

Method: Detailed written records have been kept on every birth and birth position adopted in the birth centre from January 1996 to April 2008. This data was entered into SPSS. Multivariate analysis is used, with covariates identified in the literature as being risk factors for perineal trauma (parity, birth weight, second stage length).

Results: A total of 6144 women gave birth in the birth centre from January 1996 to April 2008. Seven main birth positions were identified (all fours, semi-recumbent, lateral, standing, birth stool, squatting and water-birth. The all fours birth position was identified as the most popular birth position (48%). Compared to women giving birth in water, women giving birth on a birth stool (OR 1.40; CI 1.12-1.75) appear to have increased major perineal trauma and a higher rate of postpartum haemorrhage (OR 2.04; CI 1.44-2.90). Women giving birth in a semi-recumbent position had the highest incidence of Apgar scores <7 at five minutes. Midwives have preferences for certain birth positions and are more likely to favor water birth and less likely to favor semi-recumbent positions compared to obstetricians.

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Objective: Review of 99 third and fourth degree tears to determine risk factors

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Material and methods: Review of third and fourth degree tears in a total of 10898 women between July 2004 and February 2009 who delivered in the Hospital Universitario de Fuenlabrada. We have obtained from the total sample, 89 third and 10 tears of fourth-degree tears. We have considered the following variables: parity, type of delivery (eutocic, forceps or ventous), dilation hours on second stage, use of epidural and induction of parturition with prostaglandins.

Results: 75% of ruptures occurred in nulliparous and 25% in multiparous. The median of mean neonatal weight was 3,449 grams without any statistical differences with the rest of deliveries. The average minutes of expulsion were 99.5; median 75 and standard deviation 76,681. The use of prostaglandins or epidural did not influence the appearance of tears. We found a significantly increased risk of third and fourth degree tears with the use of forceps with a RR 2.88(1.78-4.66) for a third degree tear and a RR 66.08 (8.27-527.72) for a fourth degree tears. We found a RR 2.74 (1.49-5.05) for a third degree tear with the use of ventous.

Conclusions: The use of forceps and ventous was strongly associated with third degree tears. The fourth degree tear is only associated to forceps delivery.

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Caesarean section on maternal request – quo vadis?

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Aim: The rising number of delivery by caesarean sections, especially on maternal request without medical indication, is an important obstetric care issue. We wanted to assess the changes in the prevalence of caesarean sections and their indications from 2002 to 2008 in order to assess the need for further investigation.

Methods: We retrospectively assessed the indications of all caesarean sections performed at the University Women’s Hospital in Basel, Switzerland in the year 2002 and 2008 by reviewing the patients’ charts. Descriptive statistics and Chi-square tests for evaluation of significance were performed.

Results: There were 1594 deliveries in 2002, rising to 1862 in 2008. The number of caesarean sections rose from 23.6% to 29.9% (p=0.00004). There was an increase of women delivering by caesarean section on maternal request from 7.4% to 12.2% of all caesarean sections (p=0.013). The number of women reporting previous traumatic birth experience leading to the wish for a delivery by planned caesarean section rose from 8 in 2002 to 24 in 2008 (2.1% and 4.3% of all caesarean sections, respectively; not significant).

Discussion: There was a significant increase in caesarean sections from 2002 to 2008. The number of caesarean sections on maternal request more than doubled and the number of women reporting previous traumatic birth experience leading to a caesarean section tripled. Despite the small absolute number of this subgroup, the extensive somatic and psychosocial implications require further evaluation in order to optimize obstetric care and prevent such experiences.

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Placenta previa/accrete: The management of a serious obstetric condition

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Background: Placenta accreta (PA) encompasses various types of abnormal placentation in which chorionic villi attach directly or invade the myometrium. PA is a significant cause of maternal morbidity with massive haemorrhage and mortality. PA is now the most common reason for emergent postpartum hysterectomy and its incidence is rising because the frequency of caesarean sections.

Objective: We evaluated the frequency, the clinical findings, the diagnosis and the management of PA in our experience.

Methods: A retrospective study of 12 cases of PA referred to our Centre from January 2007 to December 2008.

Results: The incidence of PA was 0.27% (12/4477). 42% (5/12) of the cases were associated with placenta previa. 58% (7/12) had one or more prior caesarean section. An ultrasonographic evaluation was made. 2(17%) patients showed predictive sonographic signs as protrusion of the placenta in the bladder and increased vascularity of the uterine serosa-bladder interface. 25% (3/12) of patients made a pelvic MRI and they showed signs of PA such as myometrial thickness and bladder border loss. 50% of all patients had an haemorrhage as a complication. 17% (2/12) did not receive any treatment, 50% (6/12) needed a blood transfusion, 25% (3/12) had a conservative treatment including curettage and utero-vaginal packing, 58% (7/12) received caesarean hysterectomy.

Conclusions: Because the rising of caesarean delivery rate, there has been a marked increase in the incidence of PA in the years. Both sonography and MRI have fairly good sensitivity for prenatal diagnosis of placenta accreta. Hysterectomy is often the final solution.

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Vaginal birth after caesarean section (VBAC): Factors influencing uptake, success rate and outcome

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Objectives: This study was designed to analyze the VBAC rate and factors influencing it.

Methods: A prospective study including all consecutive women admitted to delivery suite with one previous CS for two months period. The data including demographics, maternal choice for mode of delivery, adherence to guidelines, maternal and neonatal outcomes were collected.

Results: 81 women met the criteria. 49 (60%) women chose to have VBAC. 73% (33/45) of Asian and 26% (10/35) Caucasian women opted for VBAC. The guidelines were adhered to in areas of consultant booking, discussion of mode of delivery at 36 weeks and continuous monitoring in labor. However, mode of delivery was discussed with only 18% women at booking. The emergency CS rate in VBAC group was 35% compared to 12.9% in the elective CS group. The VBAC rate was higher in women with previous VBAC (80% vs. 26%). The success rate of VBAC was 59%. The VBAC was more successful in women with BMI<30. The incidence of post partum haemorrhage was equal in both the groups. 2/49 required admission to neonatal unit in VBAC group compared to 6/32 in elective CS. Further analysis of these cases showed that these admissions were related to indication for CS rather than mode of delivery.

Conclusions: The choice of mode of delivery is influenced by ethnicity. The success of VBAC is determined by parity, previous VBAC, BMI, need for induction and augmentation. The key to success is counseling, which should include local outcome figures which are different from national figures.

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Treatment of 407 cases of severe post-partum haemorrhage in a French tertiary care centre: Clinical practices evolutions between 2004-2005 and 2007

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Objective: Each year, more than 120 women undergoing severe post-partum haemorrhage (SPPH) with persistent bleeding despite sulprostone administration are admitted in our tertiary care centre. We aimed to evaluate the changes in SPPH care before and after admission in our unit over the four past years.

Method: We ran a historical study comparing two groups of patients over two periods. For period 1, all the patients admitted during the years 2004 and 2005 were retrospectively included. For period 2 the patients treated during the year 2007 were prospectively included. Clinical practices, morbidity and mortality outcomes were compared.

Results: 257 patients were included for period 1 and 150 for period 2. Hemodynamic stage and SAPS-II were significantly better at arrival in our unit for period 2 (p<0.0001). Fibrinogen and platelets rates were higher for period 2 (p<0.05). The rate of SPPH after instrumental delivery decreased, while SPPH after caesarean section increased (p<0.05). Sulprostone administration was significantly higher for period 2 (94% vs. 87%, p<0.05), as well as systematic research of genital tract laceration (90% vs. 50%, p<0.0001). The need for invasive treatment before or after admission was significantly lower for period 2 (32% vs. 46%, p<0.05).

Conclusion: Women undergoing SPPH and admitted in our tertiary care centre seem to be primarily better treated in 2007. As a consequence, a significant decrease in the need for invasive treatment is observed.

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Early elective caesarean section improves outcome of infants with gastroschisis

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Gastroschisis has remained one of the four major causes of short-gut syndrome and prolonged hospital stay. This study compared the outcome of elective caesarean section before 36 weeks (ECS) and spontaneous vaginal delivery after 36 weeks (SVD).

Methods: A retrospective analysis of infants with gastroschisis born between 1986 and 2005 at a tertiary care centre was performed. Assessment included gestational age, birth weight, associated anomalies, days of ventilation (DOV), length of hospital stay (LOH), mode of closure, complications and mortality. Statistical analyses were performed.

Results: Eighty six patients were studied. This included 23 patients who had ECS before 36 weeks and 23 patients who had SVD at or after 36 weeks. The remaining 40 patients had emergency or late caesarean section. The mean gestational age of ECS Group was 34 weeks. The mean gestational age of SVD Group was 38 weeks.

The incidence of complications was significantly lower in ECS Group than in SVD Group (p=0.0182). Primary closure without patch was significantly higher in ECS Group than in SVD Group (p=0.083). Although DOV were shorter in ECS Group (ECS 3.8 days vs. SDV 4.6 days), as well as LOH (ECS 51.6 days vs. SVD 61.6 days), the difference was not statistically significant.

Conclusion: Elective caesarean section before 36 weeks is associated with less complications and higher incidence of primary closure without patch than spontaneous vaginal delivery. It is also associated with lower duration of ventilatory support and hospital stay though not statistically significant.

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Nuchal cord and obstetrical and neonatal outcome

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The present study aimed at evaluating the influence of nuchal cord on obstetrical and neonatal outcome.

In a retrospective study we analyzed the incidence of nuchal cords and its influence on the pH-value present in the umbilical artery, on APGAR-scores after 1 and 5 minutes, on the rate of non-reassuring fetal heart rate patterns as well as on the rate of fetal blood analysis. Inclusion criteria were singleton pregnancies with normal presentation and planned vaginal delivery after 34 gestational weeks (2641 deliveries in 2006).

Nuchal cord occurred in 27.5%. When allowing for nuchal cord there were no significant differences in maternal age, duration of pregnancy, birth weight, rate of meconium staining, rate of fetal blood gas analysis during delivery as well as in the rate of non-reassuring fetal heart rate patterns.

In births with nuchal cord APGAR-scores after 1 and 5 minutes were significantly (p<0.001 and p<0.05) lower than in non-nuchal cord births, however the rate of 1-minute APGAR-scores below 7 did not differ among groups.

When nuchal cord was present at birth the pH-value in the umbilical artery after delivery was significantly lower (7.26 vs. 7.28; p<0.001) and acidosis in the newborn (pH<7.20) occurred significantly more often (16.4 vs. 9.3%; p<0.001).

Furthermore, episiotomy during delivery was performed more often when a nuchal cord was present at birth (31.1% vs. 24.1%; p<0.001).

The presence of nuchal cord is associated with a lower umbilical artery pH-value and a lower 1- and 5-minute APGAR-score.

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Birthtrack – innovative ultrasound based continuous labor monitoring

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Background: The Birthtrack TM Technology is a new ultrasound based system which continuously monitors labor progress. Abdominal transducers transmit ultrasonographic waves to sensors attached to the cervix and the fetal head. Employing ultrasound triangulation the system calculates the distance between sensors and displays a continuous partogram showing cervical dilatation and fetal head descent.

Series: The birthtrack technology has been applied to 20 women giving birth who had established regular contractions at term. Cervical dilatation was up to 7cm when sensors were fixed. Apart from one all patients had a PDA. The technology improved during the series enabling the laboring women to change their position deliberately. Manual measurements were recorded along with the sensor calculations. The concordance of both recordings was correlated with signal quality necessary to obtain a reliable cervical measurement. Good quality signal measurements were highly correlated with manual cervical examinations. Fetal head descent is usually recorded along with the cervical dilatation creating a real time partogram. Using the head sensor only is an alternative option. Recordings of the fetal head descent showed to be very reliable in our series.

Comment: Continuous monitoring of labor progress using the Birthtrack system can provide the tools to reduce the variability of manual measurements thus supporting the obstetric team in all aspects up to decision making in non-progressing labor. The bedside display enables the couple to visualize the labor process thus improving the compliance and atmosphere in the delivery room.

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Tracheal occlusion early in gestation leads to greater lung growth and improved remodeling of pulmonary arteries. A nitrofen rat model for congenital diaphragmatic hernia

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Congenital diaphragmatic hernia (CDH) is associated with lung hypoplasia and abnormal pulmonary artery development. Prenatal tracheal occlusion (TO) promotes lung growth and partial reversal of structural anomalies in animal models. Limited data exists regarding TO effects at different phases of lung development. This study evaluates the impact of early (d19, pseudoglandular phase) versus late TO (d20, cannalicular phase) in a nitrofen rat model.

Wistar rats were mated within a 1-hour interval. Nitrofen was gavage fed on d9 of gestation. On d19 and d20 fetal TO was performed, respectively. Sham-operated and untouched littermates served as controls. On d21 fetuses were harvested. Only CDH+ fetuses were included in further analyzes with a minimum of 6 fetuses per group. Unpaired t-test with Bonferroni correction was used for statistical analysis.

LBWR was significantly increased in both TO groups compared to controls with significantly higher values after early versus late TO. Ki-67 RT-qPCR confirmed significantly increased proliferation in the early TO group compared to late TO and control groups. Media and adventitia thickness (%MT, %AT) were consistently reduced in the early TO group versus controls. Compared to the late TO group %MT was significantly smaller in all, %AT in large pulmonary arteries.

Our study confirms enhanced lung growth and reversal of structural abnormalities as a Result of fetal TO in a nitrofen rat model. Effects in this model are more evident after early TO (d19) than late TO (d20). These findings support the concept of early TO for fetal CDH therapy in humans.

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Objective: Most common complication of intrauterine tracheal balloon occlusion (TO) is preterm premature rupture of membranes (PPROM) which increases the rate of neonatal morbidity and mortality. Ultra-thin fetoscopic equipment may be a method to reduce the risk of PPROM.

Material and Methods: The method based on the experience of TO we performed in 17 fetal sheep in mid-gestational age. Operation was performed at 27th week of gestation after sedation and relaxation of a fetus with CDH and the liver turned up in the thorax. The method of TO was improved using an ultra-thin sheath with 1.2mm optic to minimize the diameter of the sheath to a half. After placing the fetoscope into the trachea the optic was removed and the balloon was introduced into the trachea through the fetoscopic channel under real-time 3D ultrasound.

Results: The lung-to-head ratio was increased from 0.7 to 2. The balloon was punctuated and deflated with a 22 gauge needle under ultrasound guidance at 34+2 weeks of gestation. The fetus spat out the deflated balloon which was also detected by MRI. The patient was delivered by caesarean section at 37+3 weeks of gestation and did not display any signs of PPROM.

Conclusion: This is the first operating procedure performed worldwide when fetoscopic tracheal balloon occlusion was combined with real-time 3D ultrasound probe. Fetal tracheal occlusion using ultra-thin fetoscopic equipment in combination with real-time 3D ultrasound may reduce the risk of PPROM.
Long-term amnioinfusion through a subcutaneously implanted amniotic fluid replacement port system for treatment of PPROM in humans

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Objective: Preterm premature rupture of membranes (PPROM) is one of the leading causes of perinatal morbidity and mortality. With occurrence of pulmonary hypoplasia the risk of perinatal mortality is 80%. Repetitive transabdominal amnioinfusions for treatment of PPROM showed low benefit in case of fluid loss within 6h. We developed and report here on the Amniotic Fluid Replacement Port System (AFR-port) for continuous amnioinfusion.

Material and Methods: To prove the concept and perfect the technique, subcutaneous ARF-ports were successfully used in 24 fetal sheep. In the first human patient this system was placed after two transcutaneous amnioinfusions to the patient with PPROM at 18th week of gestation with a loss of 2 liters of infused fluid during 1h. The ARF-port (Norfolk Medical, Illinois, USA) was implanted subcutaneously for long-term saline infusion (100ml/h) into the amniotic cavity.

Results: The patient did not show any signs of amnion infection or further complications. The infusion of fluid continued until the gestation was terminated by caesarean section at 29th week of gestation due to umbilical cord prolapse. The newborn boy did not have any signs of lung hypoplasia and was successfully extubated one day after delivery.

Conclusion: This is the first report of successful use of a subcutaneously implanted AFR port system in humans for long-term amnioinfusion as a treatment of PPROM for prolongation of pregnancy and avoidance of lung hypoplasia.
The diagnosis and therapy of fetal arrhythmias

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The incidence of fetal arrhythmias is 1-2%. Most of these are benign, but some can be life-threatening, requiring interventions. This report summarizes our experience with diagnosis, transplacental therapy and postnatal outcome of fetal arrhythmia diagnosed with fetal echocardiography (FE).

Material and methods: FE was performed on suspected cardiac diseases in 1287 pregnancies. The atrial and ventricular wall motions were examined simultaneously by M-mode FE. Antenatal therapy was started according to the decision of the fetal board.

Results: 45 arrhythmias were detected: 4 sinus tachycardias (infections, twin-to-twin transufusion), 25 extrasystoles (ES; 12 ventricular, 13 atrial ES) which did not require treatment. Supraventricular tachycardia (SVT) was found in 9 fetuses (3 with fetal hydrops, 1 with congenital heart defect/CHD) and atrial flutter in 1 case. Maternal transplacental therapy was started in 6 cases (Digoxin: 3 cases, Digoxin+ Verpamil 3 cases) and direct fetal therapy was applied in 1 case. Postnatally 2 neonates required propafenon. Fetal bradycardia was diagnosed in 4 cases (2 fetal deaths, 2 complete AV blocks): maternal steroid was started in 1 case, postnatal pacemaker implantation was done in 1 case. Conclusions: ES proved to be the most common fetal arrhythmia. The prognosis of SVT is good, unless it is combined with CHD or fetal hydrops. SVT leading to fetal heart failure can be stopped with maternal transplacental antiarrhythmic therapy, even premature delivery can be avoided. The outcome of fetal bradycardia is dependent on the ventricular frequency and the underlying disease.

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Prenatal diagnosis and prenatal therapy of fetal tumors

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Fetal congenital tumors are extremely rare. The prenatal diagnosis of fetal tumors is made by ultrasound and NMR. Karyotyping is essential since certain tumors are connected with genetic disorders.

The aim of our study is to present the cases of fetal tumors managed in our Clinic for last eight years and to present the cases where prenatal tumor therapy was applied.

Methodology: There were 66 cases of fetal tumor diagnosed by ultrasound: 4 CNS, 22 neck, 2 thoracic, 23 abdominal and 16 SCC teratomas. We performed karyotyping in all cases and NMR if necessary. In three cases of diagnosed fetal neck lymphangiomas we performed prenatal therapy.

Results: All tumors were diagnosed between 13 to 40wg, abnormal karyotype was found in two cases. NMR was performed in 4 cases. Pregnancy was terminated in 39 (59.1%) cases and 27 fetuses (40.9%) were delivered. Three cases with prenatally diagnosed large multicystic neck lymphangiomas, that were closely related to the fetal airway, were treated by single intralesional injection of OK-432. Progressive decrease in tumor volume had been noticed. There weren’t any complication, and no respiratory or feeding problems in neonates. The esthetical appearance was satisfactory and the children are normal.

Conclusion: Collaborative clinical research is required to provide evidence-based knowledge about the natural history, diagnosis, management, and treatment of fetal tumors. If necessary, prenatal therapy may be essential, and prenatal intralesional injection of OK-432 might be safe and effective treatment in selected cases with large neck lymphangiomas.

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Implementation of non-invasive prenatal diagnostic of fetal RHD genotype (NIPD-RHD) into routine management of all rhesus-D-negative pregnant women

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A large number of studies have already proven that analysis of the fetal Rhesus-D (RHD) genotype of RHD-negative pregnant women is possible with high accuracy, at least in a Caucasoid population. Thus, this technique can already be considered an important alternative to invasive procedures in RHD-alloimmunized women. However, since the number of RHD-alloimmunized women is blessedly low, NIPD-RHD diagnostic services are currently restricted to specialized centers only.

A number of workers have already proposed NIPD-RHD testing of all RHD-negative pregnant women since at least one dose of RHD-prophylaxis could be omitted in 30-40% of those. Furthermore, this strategy could facilitate a comprehensive diagnostic support since only large-scale screening can lead to high diagnostic accuracy, possibly at no additional cost for health care systems. Since December 2008, we offer NIPD-RHD testing to all RHD-negative women in our hospital.

We use a triplex RT-PCR reaction to test for RHD Exon 5, RHD Exon 7 and SRY which has been validated using 28 samples from pregnancies with D-positive fetus and 20 samples with D-negative fetus from the Safe network.

In addition, we are evaluating several independent markers for the presence of fetal DNA as an internal control.

If a RHD-negative fetal genotype is predicted, RHD-prophylaxis is omitted or short time interval controls will not be performed in RHD-immunized women, respectively. From the experience of this pilot site we expect to be able to offer this service to all RHD-negative pregnant women in the Vienna area within 2009.

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Fetal and neonatal echocardiographic assessment in preterm infants with twin to twin transfusion syndrome treated by fetoscopic laser coagulation

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Objective: To assess fetal and neonatal changes in cardiac morphology and function in survivors of twin to twin transfusion syndrome (TTTS) after fetal laser coagulation of anastomoses (FLC).

Study Design: In a 2 year longitudinal, prospective study we obtained echocardiographic evaluation in 51 TTTS cases treated and delivered at our center at <34 weeks’ of gestation. Cardiac measurements and left ventricular (LV) function were determined before and after FLC and at birth. Data were analyzed according to donor/recipient twins status (n=21/30). Neonatal measurements were compared with non-TTTS controls matched for gestational age. LV hypertrophy was defined as LV septum end diastolic wall thickness >2SD for gestational age.

Results: Mean (SD) gestational age at treatment and delivery were respectively, 20±3 weeks and 31.2±2.8 weeks for TTTS infants. Before laser LV hypertrophy was observed in 68% of the recipients and occurred in none of the donors; LV function was altered in recipients in comparison with donors (LV myocardial perfusion index: 0.56±0.15 v. 0.37±0.14, p=0.001) but was comparable and normal one week after laser. At birth LV hypertrophy was present in 40% of the recipients and 24% of the donors, and significantly higher than in controls (p=0.0001 and p=0.03). Ventricular function was normal and comparable in both TTTS infants (recipients and donors) and controls.

Conclusion: In TTTS recipients LV dysfunction and hypertrophy is common. After laser LV function rapidly improves, but regression of hypertrophy is progressive. Donors rarely develop cardiac hypertrophy and only after FLC. Our findings emphasize that fetal and neonatal echocardiographic longitudinal follow-up is warranted.

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Fetal temporal lobe asymmetry revisited by MRI

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Purpose: This study aims to revisit the postmortem data on fetal brain asymmetry by reassessing the asymmetric morphology of the human fetal TL between 18 and 37 gestational weeks (GW) in vivo.

Methods: Fetal MR examinations (1.5 Tesla) of 133 fetuses without structural brain abnormality (mean age 27.5 GW) were retrospectively analyzed. The length of the TL (TLL) was measured bilaterally on sagittal T2-weighted (w) sequences using the Image J software by defining an equilateral triangle, formed by the superior and inferior TL borders and measuring TLL as the distance to the tip of the temporal pole (TP). Moreover TP length, the height of the TL (TLH) and the sulcal depth of the forming superior temporal sulcus (STS) were measured on coronal T2w sequences.

Results: A paired t test showed significant right/left hemispheric differences of TLL and TPL (p<0.001). 31 (72%) cases showed a longer left TLL, compared to 12 (28%) cases with longer right TLL. The TLH (p=0.009) and the STS (p<0.001) were significantly higher/deeper in the right hemisphere. Before sulcus formation the right temporolateral cortex appears more flattened compared to the “rounded” shape of the lateral left TL. The right sided STS formed earlier than the left STS and was found to be deeper in 59, equal in 11 and shallower in 3 cases compared to the left TL.

Conclusion: Asymmetry of the fetal temporal lobe could be shown in vivo with earlier structural maturation of the right side (STS) and larger dimensions/capacity of the left. Clinical and imaging follow up correlations are currently performed in order to relate the maturational hemispheric “gradient” to brain function.

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Fetal programming of hypertension: Decreased compliance and low IGF-I plasma levels in umbilical arteries of infants with intrauterine growth restriction

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Epidemiological studies link intrauterine growth restriction (IUGR) to hypertension in adulthood. Intrauterine stress may induce lower arterial compliance that persists after birth and predisposing for hypertension in adult life. We compared umbilical arteries from IUGR (n=12, <5th percentile) vs. appropriate for gestational age (AGA) infants (n=12). Vessel wall thickness and stiffness were determined in umbilical artery vessel rings. Vessel wall elastin was quantified by elastin extraction. Cord blood was assayed for growth factors known to modulate vessel wall matrix.

IUGR infants had decreased umbilical artery compliance with an increased resistance-index (p<0.05). The vessel wall area of umbilical arteries in the IUGR group was significantly smaller than in the AGA group (2.8 vs. 3.8mm², p<0.05). Myographic measurements showed that maximal tension [mN/mm] and maximal force [mN] were significantly increased in IUGR arteries compared with AGA arteries (p<0.05). Serum levels of IGF-I, a regulator of elastin synthesis, were significantly lower in IUGR (p<0.01) than in AGA cord blood. IGF-I serum levels correlated significantly with maximum tension in umbilical arteries (p<0.01). We found a trend to reduced elastin content in the IUGR vessel walls.

IUGR infants possess thinner and stiffer umbilical arteries than AGA infants. Low intrauterine IGF-I serum levels may account for reduced arterial elastin at birth, thereby providing a potential link to hypertension in adulthood. Analyzes of cellular and molecular structure of vessels in IUGR will be a subject of future investigations using human umbilical arteries.

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Interventions to reduce preterm births in Germany

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Problem: Preterm birth is internationally and nationally one of the leading problems in obstetrics. In Germany actually 8.6% of pregnants are affected. Preterm birth is the leading cause of infant mortality and surviving infants have higher morbidity levels all their live. Preterm births are generating high costs. In 1998 the directors of the obstetric clinics in Berlin - Charité (Prof. Dr. Dudehenhausen) and Munich (Prof. Dr. Friese) together with an institute in Berlin established a study group to analyze possible interventions to reduce preterm births.

Assessment of problem: Epidemiological research on the risk and protective factors of preterm birth has consistently derived a set of factors, which increase the risk of preterm deliveries such as e.g. smoking, vaginal infections, stress. To emphasize of the known risk factors only the age, the social class of women and the sex of the infant are not accessible to intervention strategies.

Strategies: Here preconceptional, prenatal and antepartal interventions should be considered. To summarize we developed two programs counseling and promoting health: BabyCare (2000), a prenatal program followed by the preconceptional program planbaby in 2007.

Evaluation: Is annually done by comparing the rate of preterm births of participants of BabyCare compared to a prenatal data base. Controlled for age, parity, education level and multiples there is a reduction in the preterm birth rate of 27%. Up to now more than 120.000 participants were enrolled.

Conclusion: Preterm birth can be reduced significantly.

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Audit of a new protocol for assessment threatened preterm labor using cervical length measurement and cervicovaginal phIGFBP-1

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Objective: To audit the introduction of a new protocol for the assessment of threatened preterm labor.

Methods: In singleton pregnancies at 24-33+6 weeks of gestation, with intact membranes, documented uterine contractions (>4 every 20 minutes), and cervical dilatation <3cm, the cervical length was measured by transvaginal ultrasound. According to the protocol: (a) if CL >30mm, the woman was discharged home and referred to a dedicated preterm labor clinic; (b) if CL<20mm, the woman was admitted and given tocolysis and steroids; (c) for CLs of 20-30mm, phIGFBP-1 was tested. If phIGFBP-1 was negative, the suggested management was discharge and referral. If phIGFBP-1 was positive, management was admission, tocolysis and steroids.

Results: Between January and June 2008, 54 women fulfilled the enrolment criteria. 27 were admitted and given tocolysis and steroids; 27 were discharged. The rate of delivery before 37 and 34 weeks was 33% and 15%, respectively, in women admitted on initial assessment. The same rates were 15% and 0% in discharged women. Overall, the protocol was correctly applied in 34/54 women (63%). The rate of correct protocol application was 59% in (a), 100% in (b) and 45% in (c).

Conclusions: The new protocol allowed to consistently identify women with varying risks of preterm delivery, leading to a reduction of unnecessary admissions, tocolysis and steroids, without worsening pregnancy outcome in discharged women. The protocol compliance rate of 63% highlights the difficulties in implementing new management guidelines in clinical practice.

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Immunmodulatory effects of clinically relevant pathogens to the fetal immune system in pregnancy

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The aim of our study was to investigate the role of bacteria frequently found in cervical swabs of pregnant women causing premature delivery.

Methods: We comparatively stimulated cord blood PBMCs obtained from mature pregnancies without any genuine infection with different doses of purified LPS of E. coli, Klebsiella pneumoniae, Proteus mirabilis, Enterobacter aerogenes, Acinetobacter calcoaceticus, Citrobacter freundii and Pseudomonas aeruginosa as well as lysates of gram- positive Staphylococcus aureus, Enterococci and β-Streptococci for 4h and 36h to determine the secretion of a broad panel of immunologically relevant cyto- and chemokines.

Results: In fetal blood we found IL-6, TNF, IL-1β (pro-inflammatory-), IL-10, IL-13 (anti-inflammatory-), INF-γ, IL12p40/p70 (TH1-polarizing-cytokines), IL-8, MCP-1, MIP-1α and MIP-1β (chemokines) upon stimulation. IL-4 and IL-5 (TH2-polarizing cytokines) were released only rarely. None of the tested LPS variants activated cord blood cells for the release of TGF-β, IL-2, IL-7, IL-15, IL-17, IFN-α, GM-CSF, IP-10, VEGF, G-CSF, EGF, FGF- and HGF.

LPS of E.coli and Enterobacter aerogenosa revealed the strongest capacity for high production of cyto- and chemokines, whereas LPS of Pseudomonas aeruginosa induced only a variable, weak, delayed cytokine-release. Concerning special cinetics the TNF and IL12p40/p70 peak of release was in all tested LPS-variants after four hour incubation extremely elevated compared to 36 hours incubation. LPS of Klebsiella pneumoniae induced the most rapid cytokine secretion.

Conclusion: Different bacteria reveal different innate immune activation in cord blood and therefore may be considered as more or less aggressive and dangerous in inducing premature labor, rupture of membrane or premature delivery.

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Retrospektive analysis of the effectiveness of cervical cerclage for prevention of preterm delivery

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Background: Results of studies investigating the effectiveness of cervical cerclage are very conflicting. A number of randomized clinical trials failed to demonstrate any resulting improvement in neonatal survival or preterm delivery. In contradiction to this controversial view, there are also clinical data (and experience) showing that cerclage in the right patient with the right technique is able to achieve a significant prolongation of pregnancy. The aim of this retrospective study was to analyze the effect of prophylactic, therapeutic and emergency cerclage operations on the prolongation of pregnancy and the improvement of neonatal outcome.

Methods: The total of 64 patients who have been treated with cervical cerclage (Shirodkar) has been divided into three groups according to their indication for this operation: prophylactic cerclage (mean 18 weeks), therapeutic cerclage (mean 20 weeks) and emergency cerclage (mean 22 weeks). For each of these groups the outcome was analyzed.

Results: Patients treated with a prophylactic cerclage show a mean prolongation of 18 weeks, mean birth weight of 2969gr. and delivered during the 36th week of pregnancy. A mean prolongation of 13 weeks for those patients with therapeutic cerclage could be observed. Patients with an emergency cerclage operation had a mean prolongation of pregnancy of 9 weeks with a mean birth weight of 1896gr.

Conclusion: Shirodkar cerclage performed in an experienced centre is able to achieve a relevant prolongation of pregnancy. Operator skills and correct selection of the patients is essential. As expected, prolongation of pregnancy depends on the degree of cervical change.

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Mathematical modeling of the electrohysterogram: Understanding the origin of uterine contractions for preterm delivery prediction

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Background: Monitoring the uterine contractions provides important prognostic information during pregnancy and delivery. However, the available methods impose a compromise between invasiveness and accurate prediction of preterm delivery. The surface electrohysterographic (EHG) signal represents the bioelectrical activity that triggers the mechanical contraction of the myometrium. Previous work demonstrated the relevance of the EHG signal analysis for fetal and maternal monitoring and for the prediction of preterm delivery. However, for the introduction of diagnostic and prognostic EHG techniques in clinical practice, further insights are needed on the properties of the uterine electrical activation and propagation through the myometrium. An important contribution for studying the origin of uterine contractions in humans can be provided by mathematical modeling.

Methods: The myometrium cellular action potential and the effect of the tissues between the myometrium and the skin (volume conductor) are mathematically modeled. The EHG signal recorded at the skin surface is therefore expressed as a function of five parameters, of which two are the fat and the abdominal muscle thickness. The model parameters were estimated from EHG signals recorded noninvasively by a grid of 64 high-density electrodes on five women at term with contractions. For comparison, the abdominal fat and muscle thickness were also measured by ultrasound.

Results: The average correlation coefficient and the standard deviation between the ultrasonographic and EHG estimates were 0.94 and 1.9mm, respectively.

Conclusion: The model provides an accurate description of the EHG action potential and the volume conductor, with promising perspectives for future applications.

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The influence of maternal age and adverse events in the obstetric history on preterm birth rates

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Aim: We aimed to investigate the inter-related effects on preterm birth rate of maternal age and adverse events in the obstetric history (stillbirths, miscarriages, terminations of pregnancy, and extra-uterine pregnancies).

Material: We analyzed data from the perinatal statistics of eight German federal states of 1998–2000; n=508,926 singleton pregnancies.

Results: Overall, the preterm birth rate was 6.5%. For women with no previous live birth it was 7.2%, for women with one previous live birth it was 5.0%, and for women with ≥2 previous live births it was 6.8%. The frequency of adverse events in the obstetric history (see above) increased with maternal age. Excluding women with such adverse events in their obstetric history lead to a considerable decrease in preterm birth rates. For example, in women with no previous live births aged 22–23 years preterm birth rate decreased from 6.2% to 2.4% when women with adverse events in their obstetric history were excluded, and for women with one previous live birth aged 28–29 years it decreased from 4.2% to 1.1%.

Conclusions: Certain adverse events in the obstetric history (stillbirths, miscarriages, terminations of pregnancy, and extra-uterine pregnancies) have a pronounced effect on rates of preterm delivery, more so than maternal age. This means we may need to reconsider our ideas about the causation of preterm birth.

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Is routine caesarean section justified in premature infants?

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There has been an increasing rate of caesarean deliveries (C/S) for very low birth weight (VLBW) infants, despite the lack of consistent evidence of benefit for the infant and the increased maternal morbidity associated with C/S at early gestation. Attempts for randomized trials have failed and most available data is retrospective and lacking information on confounding variables.

Methods: This is a prospective cohort study performed to compare survival rate and incidence of severe intracranial hemorrhage grades III-IV (sICH) in VLBW infants born by C/S with those born vaginally. Study population included 1,227 infants with birth weight <1,500g, and gestational age (GA) ≥23 and <32 weeks, born at UM/JMH between January 1996 and December 2007. Data was prospectively collected and included maternal and fetal complications, duration of labor, presentation and indication of C/S.

Results: 497 infants were born vaginally and 730 by C/S. Infants born by C/S were of longer GA and more often in breech presentation (79% vs. 20%). There were no differences in survival or sICH incidence between both groups when the population was stratified by GA. Analysis of the sub-group of infants born in breech presentation (n=453) also showed no differences in outcomes. Logistic regression analysis to adjust for confounding variables did not demonstrate association between mode of delivery and the outcomes survival (OR 1.01; CI 0.71-1.44) or incidence of sICH (OR 0.8; CI 0.54-1.21).

Conclusion: The performance of C/S to improve survival or decrease sICH in VLBW infants is not supported by the Results of this large cohort study.

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Maternal glucocorticoid treatment and birth weight

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Administration of antenatal Betamethasone (BET) to women at risk for premature birth reduces neonatal mortality. Multiple courses of antenatal corticosteroids, however, may have adverse effects and long-term consequences. Methods: Pregnancy and birth data between 1996–2007 from the birth registry at Charité Campus Virchow hospital were analyzed retrospectively. The effects of maternal BET on neonatal anthropometrics (birth weight, head circumference, overall length), placenta weight, cord blood gases, Apgar scores and ponderal index were analyzed. BET exposed women who delivered between 23+5 and 42+0 weeks were compared to gestational age-matched controls: control males (n=21216), BET males (n=953), control females (n=20020), BET females (n=824). Three different dosage regimes were compared: group I (2x8mg BET every 10 days until birth), group II (2x8mg BET once) and group III (2x12mg BET once). Statistical analysis was performed using SPSS® with significance accepted for p<0.05. Results: BET exposed newborns had a significantly decreased birth weight compared to controls between 33–36 and 37–40wks in males (-269g and -228g, respectively) and between 33–36, 37–40 and >40wks in females (-245g, -328, -123g). Significant differences were also present for body lengths, abdominal and head circumference and ponderal index. The effect of BET was independent of gender. Placential weight, cord blood gases or Apgar scores were not different. All three dosage regimes produced almost the same effects. Conclusion: Maternal BET administration in women at risk for preterm delivery significantly decreased birth weight without dosage effect. Further studies are required to provide a better understanding of the mechanism of prenatal glucocorticoid treatment.

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The profile of early pathology in late preterm infants (LPI)

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Background: Infants born at late preterm gestational ages account for approximately 70% of all preterm births and are at risk for early and long-term morbidity.

Objective: To assess the incidence of pathology and the need and type of early medical interventions among LPI (34 0/7 to 36 6/7 weeks).

Methods: We analyzed the electronic data of all LPI born in our tertiary care perinatal center who needed admission to the NICU during the period of 2003–2007 (5 years). Infants with anomalies incompatible with life were excluded from the analysis.

Results: 585 LPI were admitted during the 5 year period, 310 (52.9%) were male and 275 (47.1%) female. Table 1 indicates the most significant reasons for admission.

Conclusion: Our data confirms the fact that late preterm deliveries carry a significant risk for neonatal morbidity. These newborns require careful evaluation immediately after birth and frequent admissions to the NICU for specialized care.

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Borderline ventriculomegaly of fetal nervous system: diagnosis and management

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Borderline ventriculomegaly is defined as a later ventricular diameter ≥10mm but ≤15mm. It occurs bilaterally in 0.15–0.7% of pregnancies and unilaterally in 0.07%. It is associated with an increased risk of chromosomal abnormalities, congenital anomalies, infections and childhood developmental delays.

The aim of this study is to evaluate the management and the diagnostic approach of fetuses with mild cerebral ventriculomegaly. We followed 52 pregnancies with a fetal borderline ventriculomegaly from 19 to 36 weeks of gestation. All patients were submitted to TORCH complex screening, kariotype analysis, genetic and neurological counseling. A careful ultrasonographic surveillance with multiplaning software was performed until delivery. When other anomalies were suspected, magnetic resonance was required. All babies were submitted to ultrasound evaluation at birth and after three months. 10 patients underwent to magnetic resonance that confirmed the presence of associated cerebral anomalies. 34 fetuses had an unilateral ventriculomegaly (diameters range 9.8–12.8mm). This sign spontaneously regressed in 10 cases during gestation. In the other case newborns had a good Apgar score at birth and the transfuntanellar ultrasound examination showed mild isolated ventricular dilatation that disappeared at the third month of life. In the other 8 cases ventriculomegaly was bilateral. One of these patients presented CMV infections that determinate a fetal death.

Isolated unilateral ventriculomegaly with diameters <12mm are usually associated with a better prognosis. Postnatal evaluation and care may be coordinated by appropriate pediatric specialists.

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Assessment of myocardial function in fetuses based on speckle tracking algorithm

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Velocity Vector Imaging (VVI) is a non-Doppler imaging modality allowing offline assessment of longitudinal, circumferential and radial dynamics of the fetal heart, independently from insonation angle. Fetal echocardiographic examination data were collected from a singleton pregnancy in 29+6 gestational weeks with normal ultrasonographic findings. Myocardial function was analyzed in 2D four-chamber view utilizing syngo VVI 2.0 software. Endocardial surface of the left ventricle was traced at beginning systole for three cardiac cycles identified by m-mode. Regional myocardial function and peak systolic values were determined by examining the longitudinal velocity (V=cm/sec), strain (S=%) and strain rate (SR=1/sec) for septal base wall V=3.421, S=-17.086, SR=-1.376; basal free wall V=2.473, S=-9.019, 028; mid free wall V=1.510, S=-23.806, SR=-1.883; mid septal wall V=2.415, S=-33.632, SR=-3.072; apical free wall V=0.178, S=-20.619, SR=-1.613; apical septal wall V=1.063, S=-9.948, SR=-0.932 and apex: V=-0.212, S=-7.564, SR=-0.712. Peak velocities and maximal displacement were found to increase from apical to basal wall segments. There was a non-homogenous distribution of shortening among the points of interest whereas the greatest strain occurred at base septal base and free wall. We used VVI to assess myocardial deformation and mechanical function as opposed to tissue Doppler–derived parameters. LV regional function in fetuses may provide a useful modality for evaluating fetal cardiac function in the future in addition to fetal Doppler.

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The relationship between sonographic transverse diameter of fetal thymus and intraamniotic infection in women with preterm premature rupture of membranes

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Objectives: A small fetal thymus may be considered a reliable sonographic marker of intraamniotic infection and fetal involvement in the inflammatory response. Some authors used the thymus perimeter. The perimeter of the thymus is difficult to define and its measurement takes a lot of time. The transverse diameter of the thymus can be defined more consistently, and is therefore more readily measurable, because the interface between the thymus and the lung are well identified.

Material and methods: We measured the transversal thymic size on routine ultrasound examination from 20 to 38 weeks’ gestation. The thymus detection rate was 96% (252 of 262 fetuses). We enrolled 43 patients between 24 and 34 weeks of gestation with preterm prelabor rupture of membranes (PPROM) in our study. Measurement was possible in 42 fetuses.

Results: In our group of women with PPROM, 13 women (31%) had histological signs of inflammation; 8 had amnionitis (19%), 4 had chorioamnionitis (10%) and 1 woman had funisitis (2%). A small thymus transverse diameter (<5th percentile for gestation age) was recorded in group with histological signs of inflammation in 92% (12/13). A small thymus showed high sensitivity and specificity (91% and 100%) for histological sings of inflammation.

Conclusions: A normal sized thymus might be useful in ruling out latent intrauterine infection. A small transversal thymic diameter is associated with acute inflammatory changes in all placental tissue samples, and not only with chorioamnionitis and funisitis.

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Nuchal translucency volume measurement in the first trimester of pregnancy using three-dimensional ultrasound

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Introduction: Three-dimensional ultrasound has already proven to be useful and reliable in nuchal translucency measurement, reducing the scanning time and providing successful measurements when two-dimensional measurement is inadequate because of unfavorable position of the fetus. Small deviations in the nuchal translucency probably cause bigger differences in nuchal volume, providing a more sensitive screening method for Down syndrome.

Objective: The objective of this study was to investigate the feasibility of measuring the nuchal volume in the first trimester of pregnancy with three-dimensional ultrasound.

Subjects and methods: Thirty consecutive women with uncomplicated singleton pregnancies attending for Down syndrome screening at 11–14 weeks of gestation were examined with a three-dimensional ultrasound device (Kretz Voluson 730, GE Healthcare, United Kingdom). The three-dimensional volume scan was stored. Using a rotational multi-planar volume measurement program (VOCAL) the nuchal area was reconstructed using a rotational angle of 15° for volume calculation.

Results: The nuchal volume of 26 fetuses (86.7%) could be calculated. The mean nuchal volume was 0.221cm³ (±0.119).

Discussion: The successfulness of nuchal volume calculation is highly dependent on the image-quality. Because reconstruction of the nuchal volume is three-dimensional, midsagittal position of the fetus is not necessary, providing advantages in deviant fetal positions.

Conclusion: This study shows that it is possible to calculate the volume of the nuchal translucency.

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Borderline ventriculomegaly of fetal nervous system: diagnosis and management

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The aim of this study is to evaluate the management and the diagnostic approach of fetuses with mild cerebral ventriculomegaly.

We followed 52 pregnancies with a fetal borderline ventriculomegaly from 19 to 36 weeks of gestations. All patients were submitted to TORCH complex screening, kariotype analysis, genetic and neurological counselling. A careful ultrasonographic surveillance with multiplaning software was performed until delivery. When other anomalies were suspected, magnetic resonance was required. All babies were submitted to ultrasound evaluation at birth and after three months. 10 patients underwent to magnetic resonance that confirmed the presence of associated cerebral anomalies. 34 fetuses had an unilateral ventriculomegaly (diameters range 9.8–12.8mm). This sign spontaneously regressed in 10 cases during gestation. In the other case newborns had a good Apgar score at birth and the transfuntanellar ultrasound examination showed mild isolated ventricular dilatation that disappeared at the third month of life. In the other 8 cases ventriculomegaly was bilateral. One of these patients presented CMV infections that determinate a fetal death.

Isolated unilateral ventriculomegaly with diameters < 12 mm are usually associated with a better prognosis. Postnatal evaluation and care may be coordinated by appropriate pediatric specialists.

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First trimester screening and fetal karyotyping with screening for fetal cardiac abnormalities by nuchal translucency: The value of sonography in early pregnancy

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Purpose: The objective of this study was to determine the fetal aneuploidy at 11-14 weeks of gestation and examine the ability to detect cardiac defects with increased nuchal translucency thickness at 11–14 weeks of gestation.

Material and Methods: 956 women at 11–14 weeks of gestation participated in this study. Screening was performed by calculating the risk from maternal and gestational age which was adjusted with the nuchal translucency measurement and maternal serum biochemical markers. An adjusted risk of >1:270 was considered as a positive screening test. Pregnancies with the adjusted risk over the 1:270 value were advised about fetal karyotyping. In cases where the nuchal translucency was >3.0mm, cardiac scans were performed by an expert in fetal echocardiography. This was carried out at 18–22 weeks of gestation.

Results: Screening was positive in 21% of fetuses (203/956) when the adjusted risk was more than 1:270. Fetal karyotyping was determined prenatally in 123 out of 956 cases (12.9%). The second trimester anomaly scans carried out on the fetuses with normal karyotype and in the case of aneuploidy did not show persistent nuchal oedema. One case of stenotic pulmonary trunk and one case of ventricular septal defect were found. As a Result it was also effective to measure nuchal translucency to determine cardiac anomaly for screening (2/203 1% vs. 5/756 0.66%).

Conclusion: In our Results, screening for fetal aneuploidy by maternal age, nuchal translucency and serum marker measurements can be effective for the detection of cardiac abnormalities.

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Sonographic findings of isolated spina bifida diagnosed in utero and two years follow-up

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Objective: To identify prenatal prognostic criteria in cases of spina bifida.

Materials and Methods: A retrospective study of cases with spina bifida between 2001 and 2006 referred to the Department of Gynecology and Obstetrics at the University of Münster. Prenatal findings (Arnold Chiari Malformation (pACM), lesion segmental size (pS), lesion high (pH), foot position (pF), cisterna magna (CM), ventriculomegaly (pV), posterior ventricle size (HSVp), anterior ventricle size (HSVa)) and postnatal and two year follow-up data were correlated (muscle tone postnatal (M)/two years (M2), patellar reflex two years (PSR2), achille reflex two years (ASR2), leg movement postnatal (L1)/two years (L2), foot position postnatal (F1)/two years (F2), walking two years (W2), arnold chiari malformation (ACM), ventriculomegaly postnatal (V1)/two years (V2), Shunt postnatal (S1)).

Results: In 53 fetuses spina bifida was diagnosed and detailed follow-up was available in 17 cases. There was a significant correlation between prenatal diagnosis and postnatal data. Prenatal findings of low lesions, small lesion size, a regular foot position, the absence of ventriculomegaly and regular CM, HSVp or HSVa were independently related to a good postnatal prognosis. There was no association between pACM and postnatal outcome.

Conclusion: Prenatal ultrasound findings are associated with postnatal outcome. This correlation helps to advise patients with regard to prognosis in cases of spina bifida. Long-term follow-up is needed to allow for a better evaluation of these issues as well of neurological outcome.

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Incidence of skeletal abnormalities in a prenatal diagnosis unit

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Objectives: To know the incidence of skeletal abnormalities in 53,320 pregnant women who were evaluated in a prenatal unit in a period between 1980–2008.

Material and methods: A group of pregnant women (53,320) were sonographically controlled in a randomized selection.

For the evaluation we used different ultrasound equipments: 2D, 3D & 4D.

Results: (See Table #1)

Conclusions: Skeletal abnormalities are the less common findings and represents 1.5% of the total anomalies that we detected in this period.

Ultrasound plays an important role to detect this kind of fetal pathologies.

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3D reconstruction of the female pelvis to estimate the distance between the infrapubic line and the plane of ischial spines

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Assessing fetal position during second stage of labour is improved by translabial ultrasound. Besides digital vaginal examination a translabial ultrasound plays an important role by documenting fetal station and progress. New software Sono-VCAD in labour presented by GE Healthcare uses 3-dimensional (3D) ultrasound to propose the possibility of different planes to evaluate fetal position in conjunction with maternal symphysis pubis. The new software allows measuring fetal head direction, the angle of progression and fetal head progression relating to a line through the long axis of the symphysis pubis and a line perpendicular to it (infrapubic line). To estimate fetal head progression and to be able to compare it to digital vaginal examination the relation between the infrapubic line and the plane of ischial spines in the sagittal view is essential.

Method:
As published by Henrich et al. 2006 computer tomographic 3D reconstructions of normal female pelvises were evaluated in the midline sagital view. We measured the distance between the infrapubic line and ischial spine of 27 women between 25 and 45 years of age.

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Measurement of fetal urine production by three-dimensional ultrasonography in normal pregnancy

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Objectives: Amniotic Fluid Index (AFI) is considered an important marker of fetal well-being. The aim of this study is to measure bladder volume and to establish a correlation between urine production rate (UPR) with AFI and PSV (Peak Systolic Volume) of the renal artery.

Methods: 31 cases of normal singleton pregnancy without medical or obstetric complications were collected, the gestational age of pregnancies was between 20° and 22° weeks. 3D Ultrasound scans have been performed with Voluson E8 (GE Healthcare, USA). The method to obtain volume measurement from 3D volume datasets is VOCAL (GE Medical System, Austria). We defined the bladder surface contour with rotation steps of 30° angle on the reference plane. The surface contour is defined at each step: Bladder volume was calculated after all contours traced. To calculate the rate of fetal urine production, we measured bladder volume at intervals of 5mins: UPR (mL/h) = (second bladder volume – first bladder volume) x (60/x). X means time interval (mins) between bladder volume measurements. Bladder volume was measured three times.

Results: The mean of urinary production (UPR) rate was 3.53ml/h, according with the literature. We demonstrated the correlation between UPR and both RI and PSV of renal artery (p<0.05). We couldn’t find out a significative relation between UPR and AFI (p=0.750).

Conclusions: Measurement of fetal urine production may be an alternative to AFI or single deepest pocket, in alternative to AF volume measurement to evaluating fetal hypoxia.

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Uterine artery doppler velocimetry during first trimester of pregnancy to predict decreased endovascular trophoblast invasion associated with adverse pregnancy outcomes

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Objective: Successful placentation relies on normal trophoblastic invasion of the maternal decidua, myometrium and blood vessels. Uterine perfusion appears to regulate uterine receptivity. This article investigates the relationship between Doppler studies of uterine artery and endovascular trophoblastic invasion in the first trimester of pregnancy.

Methods: Doppler ultrasound examination of the maternal uterine arteries was performed in women attending for termination of pregnancy for non-medical reasons. We recorded the Doppler flow velocity waveforms using a Shimadzu 2000 ultrasound machine with a 3.5 or 5 MHz probe. Colour Doppler ultrasound was used to identify the main branch of the uterine artery at its junction with the internal iliac artery, from where we obtained blood flow velocity waveforms. High-resistance cases were defined as those presenting with bilateral or unilateral uterine artery notches and a mean RI above the 95th centile. The conceptional products were examined histologically with regard to the extend of decidual endovascular trophoblast invasion.

Results: At the week 8, there were 19 high-resistance and 17 low-resistence uterine artery blood flow. The proportion of decidual vessels with endovascular trophoblast invasion was significantly higher in the low-resistance pregnancies (65%) compared with high-resistance ones (47%; p=0.18).

Conclusion: Interstitial invasion, deeper decidual-myometrial junction invasion and the release of vasoactive mediators may explain changes in arterial resistance and be related to decidual endovascular trophoblastic invasion.

Doppler ultrasonography is a non-invasive method for evaluating trophoblastic invasion in early pregnancy. Further studies are necessary to clarify the significance of these observations.

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Uterine arteries’ Doppler mediation at 20 weeks of gestation and perinatal outcomes

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Objectives: To determine if there is relation between a pathological uterine arteries’ Doppler detection at 20 weeks of gestation, the follow-up of its changes and the subsequent appearance of perinatal complications.

Material and methods: Prospective longitudinal study with statistical computerized analysis with SPSS-PC+.

Applying some exclusion criteria, finally 1169 ultrasound scans of second quarter practiced in our hospital during the year 2008 are analyzed. Many variables are valued: pathological obstetric precedents, uterine arteries’ Doppler mediation in different moments (pathological if average pulsatility index >p95), percentile of estimated weight by ultrasound, information of the childbirth, hospitable incomes in Neonatology’s unit and reasons.

Results and conclusions: A pathological uterine arteries’ Doppler at 20 weeks (even if normalized after) is associated to worse perinatal outcomes, with lower percentile of estimated weight by ultrasound in the third quarter (p=0.001), lower weight of the newborn (p=0.000), less weeks of gestation at the childbirth (p=0.03) and lower Apgar in the first minute of life (p=0.042). Pregnancies with normal uterines’ Doppler in the third quarter have statistically significant differences in the percentile of estimated weight by ultrasound in the third quarter (p=0.001) and the weight of the newborn (p=0.000), weeks of gestation at the childbirth (p=0.023) and Apgar in the first minute (p=0.027), depending on the affectation of this Doppler at 20 weeks. This supports the hypothesis of that detecting a pathological uterine arteries’ Doppler in the second quarter could be a precocious scoreboard of small fetuses for gestational age and/or intrauterine restricted growth.

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Correlation between quantitative three dimensional Doppler parameters and real blood flow within the utero-placental unit: evaluation in a pregnant sheep experimental model

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Objectives: To evaluate the correlation between 3D Doppler parameters and blood flow within the utero-placental unit in a pregnant sheep model.

Methods: Nine pregnant sheep carrying singletons were used. The pregnant horn was exposed. A flow quantitative sensor allowing real time assessment of the blood flow and a controllable vascular occlusion system were then placed around the common uterine artery, while all the others uterine arterial supplies were ligated. Several occlusion levels were applied. 3D Doppler acquisitions of placentomes were concomitantly realized with the ultrasound probe placed directly in contact with the larger curvature of the pregnant horn. Acquisition parameters were standardized. Each placentome was rebuilt 3-dimensionally using the VOCAL software. The correlation between real vascular flow within the uterine artery as measured with the flow sensor and 3D Doppler parameters was evaluated.

Results: All the 3D Doppler parameters were significantly correlated with the real vascular flow measured concomitantly by the flow sensor. A higher correlation degree was observed for VI and VFI (r = 0.86 and 0.82 respectively p<0.0001) than for FI (r = 0.64; p<0.0001).

Conclusion: To our knowledge, this is the first in vivo experimental study confirming a significant correlation between real blood perfusion and quantitative three-dimensional Doppler parameters measured within the utero-placental unit. These Results confirm the potential great interest of the use of 3D Doppler ultrasound for the assessment for placental vascular insufficiencies in clinical cases and in a research set-up, to evaluate placental blood flow in sheep models of intra-uterine growth retardation.

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The use of placental growth factor (PIGF) in maternal serum and the uterine artery Doppler pulsatility Index (PI) for the prediction of perinatal outcome in gestations complicated with IUGR and PE

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Objective: To evaluate the combination of Uterine artery Doppler PI and PIGF in maternal serum, for the prediction of perinatal outcome in intrauterine growth restricted fetuses and preeclampsia.

Material and methods: This is a longitudinal prospective case control study, that lasted 24 months. We included gestations complicated with small for gestational age fetuses (SGA), intrauterine growth restricted fetuses (IUGR), hypertension and/or preeclampsia (PE) where uterine arteries Doppler PI and PIGF were determined at the time of diagnostic. We followed up 500 gestations and their perinatal outcome.

Results: Significant differences of uterine arteries Doppler IP and maternal serum concentration of PIGF (p<0.01) were observed between gestations with PE and/or IUGR fetuses and controls. These differences were not observed in gestations with SGA fetuses or hypertension. We also found significant differences of uterine artery Doppler PI and maternal serum concentration of PIGF (p<0.01) in PE or IUGR fetuses between those with adverse perinatal outcome and those with normal perinatal outcome.

The combination of uterine artery Doppler IP and concentration of PIGF did not improve the prognosis of adverse perinatal outcome due to PE and/or IUGR comparing with the use of uterine artery Doppler IP alone.

Conclusion: Uterine arteries Doppler IP in third trimester allow us to select a group of patients with a highest risk for adverse perinatal outcome due to PE and/or IUGR. Concentration of PIGF in third trimester does not improve the Results of uterine arteries Doppler IP but could be a good alternative with similar Results.

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Vascularization of the placenta and the sub-placental myometrium: Feasibility of a three dimensional power Doppler ultrasound quantification technique

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Objective: The objective of this study was to assess the feasibility of placental and myometrial volumes and vascularization assessment using 3-D ultrasonography.

Design: Prospective observational study.

Setting: A French teaching hospital.

Patients: Thirty eight patients undergoing normal pregnancies.

Interventions: 3D standardized acquisitions were performed in the mid part of the utero-placental unit, once between 15 to 39 weeks.

Main outcome measures: Volume and vascularization parameters (VI, FI and VFI) of placenta and myometrium were measured. Intra & inter-observer reproducibility were evaluated.

Results: volume and vascularization measurements respectively presented an Intra-class Correlation Coefficient of at least 0.96 & 0.79 for intra-observer, and 0.78 & 0.92 for inter-observer reproducibility. Placental measured volume shows a significant rise in the third trimester when compared with the second trimester (107.937 vs. 149.396; p 0.07), whereas no significant difference is observed for VI, FI and VFI. Concerning the myometrium, we observed no significant difference between second and third trimester for volume and FI. However, VI (28.090 vs. 19.374) and VFI (17.691 vs. 11.336) were significantly lower in the third trimester (p 0.01).

Conclusion: 3D quantification of placental and myometrial volumes and vascular parameters is feasible with a high intra and inter-observer reproducibility. This technique might be of great interest for the diagnosis and/or screening of uteroplacental insufficiencies and should therefore be evaluated in clinical observational studies.

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Chronic hypertension: correlation of umbilical artery doppler evaluation and perinatal results

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Introduction: Chronic hypertension is a placental insufficiency situation where Doppler evaluation may help to determine fetal hypoxia.

Material/Methods: The 123 umbilical artery Doppler evaluations in patients with chronic hypertension, followed between 2005–2008, were selected. We evaluated: fetal biometry, umbilical artery Doppler [classified into 3 groups: I-normal, II-with resistance index≥P90 for gestational age (GA) and III-with absent telediastolic flux]; middle cerebral artery (MCA) Doppler; GA at delivery; newborns birth-weights and admission to neonatal intensive care unit (NICU).

Results: In group I (n=108), 67% of patients were under anti-hypertensors; there were 10.1% of intrauterine growth restriction (IUGR); c-section was performed in 56% at 37.6±3.3 weeks and NICU admission was needed in 10.1% of the newborns.

In group II (n=7), 71.4% were under anti-hypertensors; there were MCA signs of centralization in 57.1% (with no significantly differences regarding newborns outcomes between those with or without centralization) and 85.7% of IUGR [p<0.0001; OR 53.5(95%Clt; 5.9-485.7) when compared to I]; delivery was by c-section in 100% at 34.0±3.0 weeks (p<0.0001, compared to I) and NICU admission was needed in 71.4% of the newborns [p<0.0001; OR 22.3(95%Clt; 3.8-128.7) when compared to I].

In group III (n=8), all patients were under anti-hypertensors; there were 62.5% of IUGR [p=0.001; OR 14.8 (95%Clt; 3.1-70.7) when compared to I]; delivery was by c-section in 100% at 32.1±3.5 weeks (p<0.0001, compared to I) and NICU admission was needed in 87.5% of the newborns [p<0.0001; OR 62.4(95%Clt; 7.0-555.0) when compared to I].

Conclusions: An altered umbilical artery Doppler in patients with chronic hypertension has a strong correlation with adverse perinatal outcomes, namely with lower GA at delivery, IUGR and admissions of newborns to NICU.

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Is it color Doppler avaluable in pregnancy induced hypertension?

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Introduction:
Objective: To evaluate the role of Color Doppler in predicting the fetal outcome in cases of pregnancy induced hypertension (PIH)
Materials & Methods: A total of 756 cases of PIH between 28 -37 weeks of gestation were studied in a period of February 2004-February 2009. A color doppler scanner with a 3 - 5 MHz curvilinear probe was used for studying umbilical & fetal middle cerebral arteries. We used the value of PI as the indicator to evaluate perinatal outcome. The Results of first doppler examination were taken into consideration for the study. Follow up study was done whenever required. The value of PI more than 95th percentile in umbilical artery & AEDV or REDV and the ratio C/P <1 was considered abnormal. The Results were correlated with parameters of fetal outcome.
Results: In our study of 756 hypertensive cases 58% had abnormal PI in umbilical art 61% of these patients delivered IUGR babies. In patients with absent end diastolic velocity (AEDV) & reversed end diastolic velocity (REDV) perinatal mortality was 49% & had IUGR babies. The fetuses with compromised circulation showed increased diastolic flow in fetal MCA suggestive of brain sparing effect. The Results of abnormal umbilical artery were more significant than brain sparing in predicting perinatal outcome.
Conclusion: Color Doppler is an excellent tool for non-invasive hemodynamic monitoring of PIH patients. It helps to identify the fetuses at risk & predict perinatal morbidity & mortality. Doppler velocimetry can guide us in the treatment of these pregnancies & prevention of high mortality & morbidity in hypertensive patients
Keywords: Pregnancy induced hypertension, Color Doppler & IUGR.

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Ophthalmic artery resistive index in preeclampsia prediction of fetal centralization

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Background: Maternal and fetal manifestations of preeclampsia are usually non-parallel. Evidence of fetal distress, especially fetal centralization, is a relevant predictor of adverse outcomes. The purpose of this study was to verify the association between maternal ophthalmic artery resistive index (OARI) and the ratio between pulsatility indexes in umbilical artery (UAPI) and middle cerebral artery (MCAPI) - the umbilical-cerebral ratio (UCR) - in mild and severe preeclampsia. Fetal centralization was defined by UCR>1.

Methods: Sixty-four women with mild preeclampsia and 88 with severe preeclampsia participated in this study. Correlation between OARI and UCR were obtained using Spearman’s correlation index. A ROC curve for fetal centralization was obtained according to OARI measurements. The cutoff point for the prediction of fetal centralization in function of OARI was obtained.

Results: Fetal centralization was respectively identified in 10 (15.6%) women with mild preeclampsia and 32 (36.4%) women with severe preeclampsia. No difference in gestational ages was obtained between women with mild and severe preeclampsia (33±3 and 34±4, p=0.454). OARI presented a significant inverse correlation with UCR (r=-0.679, p=0.003) in women with severe preeclampsia, whereas a non significant, weak correlation was demonstrated in mild disease (r=-0.124, p=0.645). The area under ROC curve was 0.78±0.03. The cutoff point of 0.56 OARI provided 0.78 sensitivity and 0.76 specificity for fetal centralization.

Conclusion: OARI<0.56 is a relevant predictor of fetal centralization. Data suggests similar behavior in maternal and fetal central vascular beds in preeclampsia.

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Impact of parity in small for gestational age births, perinatal outcome and obstetric mother future

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Objective: The aim of this study was to assess the impact of parity in small for gestational age births, perinatal outcome and obstetric mother future.

Methods: retrospective cohort study of all livebirths between 32-41 weeks occurred in our hospital among 2000-2008. We classified as small for gestational age (SGA) all newborns with weight <10 percentile. We compared the characteristics of mothers, newborns, adverse outcomes and obstetric future between primiparas and multiparas.

Results: SGA were diagnosed in 73 primiparas and 41 multiparas, 3 cases missing. Maternal pathology and pregnancy duration were similar in both groups. The mean of maternal age was 24.6 years for primiparas and 29.8 years for multiparas.

Higher rates of emergency caesarean (50%) were found in primiparas compared to multiparas (32%). Otherwise programmed caesarean rate was higher in multiparas (27%) than primiparas (11%) (p>0.05).

There was no statistical difference in I. Apgar (1 and 5 minute), necessity of reanimation or neonatal intensive care, hospital staying and complications.

Eighteen women (12 primiparas and 6 multiparas) had another pregnancy in this period (2000-2008), six of these newborns were SGA (3 primiparas and 3 multiparas). One multipara had maternal pathology and other was drug addict. No miscarriage occurred.

Conclusion: Results indicate that increase parity is not a risk factor for SGA newborn outcome. Only 15.7% of women had another pregnancy, one third SGA reoccurred. Once the size sample was small, more studies are needed.

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First trimester screening for chromosomal anomalies

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Screening for major chromosomal anomalies can be provided in the first trimester of pregnancy. One of the traditional screening methods for chromosomal anomalies is maternal age. Using that as screening, about 5% of the population should be submitted to an invasive test (amniocentesis or cordocentesis) to confirm the karyotype, identifying approximately 30% of the fetuses with trisomy 21. Screening by a combination of fetal nuchal translucency (NT) and maternal serum human gonadotropin and pregnancy-associated plasmaprotein-A can identify 90% of the fetuses with trisomy 21 and other major chromosomal anomalies for a false positive rate of 5%. With the Combined test less than 3% of the population needs to be submitted to an invasive test.

First trimester screening can also detect other chromosomal anomalies such as trisomy 18. In addition, measurement of NT may help detect pregnancies at risk for major fetal heart defects.

The Combined test was introduced in Hospital Central Funchal in January 2008, to all pregnant women with gestational age between 11 and 13w+6d.

The authors studied the screening Results between January and September 2008. They evaluated maternal age, number of positive tests, number of amniocentesis performed for positive test and number of Down syndrome cases observed.

The correct use of first trimester screening could be a secure alternative to an invasive procedure in a pregnant woman with 35 y-r-old or more. Detecting problems earlier in the pregnancy may allow women to prepare for a child with health problems or to terminate pregnancy with lesser risks.

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Ethnic differences in deciding whether or not to participate in prenatal screening for Down syndrome

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The primary aim of this study was to describe ethnic differences in participation to prenatal screening for Down syndrome and to assess to what extent these differences can be attributed to demographic characteristics and women's considerations whether or not to participate in prenatal screening. The secondary aim was to assess ethnic differences in stages of decision-making and decisional conflict. The study population consisted of 105 Dutch, 100 Turkish and 65 Surinamese pregnant women attending midwifery or obstetrical practices in the Netherlands. Each woman was personally interviewed 3 weeks (mean) after booking for prenatal care. Actual (non-) participation in prenatal screening was assessed several months later.

In total 56% of the Dutch, 87% of the Turkish and 83% of the Surinamese women did not participate in prenatal screening. These ethnic differences could to a large extent be attributed to ethnic differences in age and acceptance of what God gives. Compared to Dutch women, Turkish and Surinamese women more often did not consider whether or not to participate in prenatal screening or did not know what to decide yet and experienced more decisional conflict at time of the interview. These findings suggest the need for improvement of counseling in order to enable all women to make a deliberate decision that is based on sufficient knowledge and personal values and beliefs.

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Information about prenatal screening for Down syndrome. 
Ethnic differences in knowledge

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The aim of this study was to evaluate the provision of information about prenatal screening for Down syndrome to women of Dutch, Turkish and Surinamese origin, and to examine the effects of this provision on ethnic differences in knowledge about Down syndrome and prenatal screening. The study population consisted of 105 Dutch, 100 Turkish and 65 Surinamese pregnant women attending midwifery or obstetrical practices in the Netherlands. Each woman was personally interviewed 3 weeks (mean) after booking for prenatal care. Most women reported to have received oral and/or written information about prenatal screening by their midwife or obstetrician at booking for prenatal care. Turkish and Surinamese women less often read the information than Dutch women, more often reported difficulties in understanding the information, and had less knowledge about Down syndrome, prenatal screening and amniocentesis. Language skills and educational level contributed most to the explanation of differences in knowledge.

Interventions to improve the provision of information to women from ethnic minority groups should especially be aimed at overcoming language barriers, stimulating women to read written material and targeting information to the women’s abilities to comprehend the information about prenatal screening for Down syndrome.

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Ethnic differences in informed decision-making about prenatal screening for Down syndrome

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The aim of this study was to assess ethnic variations in informed decision-making about prenatal screening for Down syndrome and to examine the contribution of background and decision-making variables.

The study population consisted of 105 Dutch, 100 Turkish and 65 Surinamese pregnant women attending midwifery or obstetrical practices in the Netherlands. Each woman was personally interviewed 3 weeks (mean) after booking for prenatal care. Knowledge, attitude and participation in prenatal screening were assessed following the 'Multidimensional Measure of Informed Choice' that has been developed and applied in the UK.

In total, 71% of the Dutch women were classified as informed decision-makers compared to 5% of the Turkish and 26% of the Surinamese women. Differences between Surinamese and Dutch women could to a large extent be attributed to differences in educational level and age. Differences between Dutch and Turkish women could mainly be attributed to differences in language skills and gender emancipation. Interventions to reduce these ethnic differences should first of all be aimed at overcoming language barriers and increasing comprehension among women with a low education level. To further develop diversity-sensitive strategies for counseling it should be investigated how women from different ethnic backgrounds value informed decision-making in prenatal screening, what decision-relevant knowledge they need, and what they take into account when considering participation in prenatal screening.

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The variability and specificity of PAPP-A and free β-HCG in the first-trimester down syndrome screening

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Aim: To assess the specificity of biochemical markers free β-hCG and PAPP-A during the first trimester of pregnancy and to determine the variability of maternal serum concentrations of studied markers between the 10+3 and 13+6 weeks of gestation.

Subjects: The study population comprised 2883 unaffected, singleton, non-diabetic and spontaneously conceived pregnancies. Pregnant women were separated in 4 groups, depending on the weeks of gestation when the biochemical analyzes were performed.

Methods: The concentrations of free β-hCG and PAPP-A in maternal serum were determined by solid-phase, enzyme-labeled chemiluminiscent immunometric assay (DPC-IMMULITE). Concentrations were converted to MoMs, according to centre-specific weighted regression median curves for free β-hCG and PAPP-A, obtained on daily median values for unaffected pregnancies.

Results: There were no significant differences between the sub-groups, according to the maternal age, maternal weight and the proportion of smokers. Significant difference in log10 MoM values of free β-hCG (p<0.05) was found between the 11th and 12th weeks of gestation. Significant differences were ascertained for log10 MoM PAPP-A between the 11th and 12th, as well as between 12th and 13th weeks of gestation (p<0.05). False-positive rates of biochemical risk for trisomies were 16.1% before the 11th week, 12.8% between weeks 11 and 11+6, 11.9% between weeks 12 and 12+6, and 9.9% after week 13. The differences in proportions were not statistically significant (χ²=0.813, p=0.37).

Conclusion: Although the MoM values of maternal serum free β-hCG and PAPP-A showed certain variations between 10th and 14th week of gestation, the impact on specificity of biochemical markers in study population was not statistically significant.

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Atrial septal aneurysms – prevalence, prenatal diagnosis and clinical significance

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We sought to tabulate the characteristics and relevance of antenatally diagnosed atrial septal aneurysms (ASA).

ASA are defined as redundant tissue emerging from the septum primum with abnormal bulging into the left atrium. The pathogenesis of ASA remains widely uncertain as well as their implications. Recent data suggest a prevalence among newborns to be as high as 7.6%, similar findings were previously reported in an antenatal population. ASA are often associated with premature atrial beats (36%), likely to be induced by cyclical contact of the redundant flap with left atrial wall. A direct correlation of the degree of bulging and the severity of atrial arrhythmias has been postulated. An association with abnormal karyotypes has not been confirmed yet.

A recent prospectively conducted study revealed a spontaneous resolution rate of ASA of 69% within 1 month and a complete resolution at the end of the first year of life. Fetal atrial arrhythmias caused by ASA tend to disappear within the first 3 months following delivery. In case of fetal ASA no complications related to the lesion have been documented neither there were any indications for antenatal treatment, suggesting ASA to be a benign and transient lesion.

On the contrary persistent ASA and/or PFO preferentially diagnosed during later life are potential risk factors for severe disease manifestations, particularly thrombus formation. Lifelong administration of anticoagulative drugs has been recommended. Facing the further decreasing mortality related to surgical approaches it seems reasonable to consider minimal invasive surgical treatment modalities.

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Cervical pregnancy complicated by placenta accreta in the first trimester

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Placenta accreta refers to an abnormal adherence of the placenta to the uterus with subsequent failure to separate after delivery. The majority of cases of placenta accreta are identified intraoperatively at time of delivery.

Placenta accreta occurs in the first trimester, so pregnant women who have a history of previous dilatation and curettage, more a previous Cesarean section and a low lying gestational sac should be carefully screened.

We report a case report of placenta accreta diagnosed in the first trimester. Pregnant of 26 years old, with a previous caesarean section, presented with a cervical pregnancy. The gestational age was 9 weeks, a viable embryo was present.

Color Doppler ultrasound showed hypervascularity located between the placenta and the underlying myometrium, formed vessels at the serosa–bladder border, no miometrial thickness was detectable between bladder and gestational sac. These findings were confirmed using 3D power Doppler.

Conservative treatment with metotrexate systemically was chosen after a informed consent. For the failure of medical treatment the patients had underwent dilatation and curettage and Foley catheter insertion after D&C.

After 24 hours, while was removed Foley catheter there was been severe hemorrhage and the patient was underwent hysterectomy. The uterine serosa appeared hypervascular over the lower uterine wall, yet no evidence of bladder involvement was observed.

Ultrasound findings (gray ultrasound, 3D power Doppler and Color Doppler) in the first trimester can suggest the diagnosis of placenta accreta.

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Contribution of fetal MRI in the antenatal diagnosis of intracranial hemorrhages

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We report sixteen ecographic suspected fetal intracranial hemorrhages studied in utero in fetuses with gestational ages ranging from 20 to 37 weeks. In all of them a detailed evaluation with magnetic resonance imaging (MRI) was performed in an attempt to confirm either reject the antenatal diagnosis. Abnormal signs showing brain injuries were identified: five germinal matrix hemorrhages, one posterior cerebral fossa hemorrhage, three intraparenchymal hemorrhages, three intraventricular hemorrhages, one choroidal plexus hemorrhage and three cerebellar hemorrhages. Postnatal follow-up was obtained in all cases comparing MRI Results with exploratory findings in order to verify diagnostic accuracy of prenatal MRI for the prediction of this kind of cerebral pathology.

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Additive value of MRI in prenatal diagnosis of central nervous system malformation

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Malformations of the central nervous system (CNS) are among the most frequent congenital anomalies. Ultrasonography (US) is the screening modality of choice for evaluation of the fetal CNS. MRI frequently adds additional information beyond ultrasound. Between 01/2005 and 03/2009 in our tertiary fetal medicine referral center twenty-one pregnant women with fetal CNS malformations detected by obstetric US a fetal MRI was performed. The aim of the study was to find out, if MRI adds supplement value information. Therefore the Results of US and MRI were compared to postnatal outcomes or - in case of termination of pregnancy (TOP) - neuro-post mortem analysis and the additive diagnostic value was assessed. In most cases MRI confirms the Results of the US examination, but in a few cases, the MRI detected malformations, which were not obvious in US screening. On the other hand, especially in early pregnancies, US is superior to MRI, due to the fact that the MRI exam is limited due to fetal movements and inappropriate slice thickness. As shown in our case series prenatal US is the primary screening modality for the evaluation of fetal CNS malformation. In some cases MRI currently serves as a second line imaging tool by adding valuable information supplemental to ultrasound examination e.g. in case of late gestational age, adverse fetal position, oligohydramnion and increased maternal body mass index. The additional use of MRI following ultrasound screening allows better prenatal diagnosis and therefore counseling of parents in a multidisciplinary setting.

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Presence or absence of TTTS in twin pregnancies: Are there differences in placental pathologies seen by fetal MRI?

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Introduction: Twin-twin transfusion syndrome (TTTS) is a severe complication of monochorionic pregnancies. Arterio-venous anastomoses are thought to be responsible for the unbalanced inter-twin blood flow. The purpose of this study was to evaluate whether differences in the placental parenchyma due to TTTS can be seen in fetal MRI.

Material and Methods: In a retrospective study 34 monochorionic pregnancies between gestational weeks 17 and 32 with placental pathologies on MRI scans were investigated on a 1.5 Tesla MR. 17 pregnancies were affected by TTTS, 17 showed no clinical signs of TTTS. 5 TTTS cases were treated with Laser coagulation of communicating vessels. Placental maturation and pathologies, as well as differences in placental diffusion, were investigated.

Results: 100% of the 17 pregnancies affected by TTTS showed abnormal placental maturation, as well as 64% of the non-TTTS group. 70% of placentas with TTTS showed infarctions, and 47% without TTTS, respectively. 47% of placentas with TTTS showed differences in diffusion, as well as 41% in the none-TTTS group. Intrauterine growth restriction (IUGR) rates were 41% (TTTS) and 50% (non-TTTS), respectively.

Discussion: TTTS is correlated with higher rates of placental infarction. It seems as if TTTS or its treatment influences the maturation process of the placenta, as none of the patients had a normal maturation on MR scans. Differences in diffusion were found, but allocation of placental parenchyma to each twin was not possible. IUGR rates were high in both groups.

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The significance of an absent fetal stomach on second trimester ultrasound

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Background: We sought to examine the diagnostic and prognostic implications of the finding of an absent stomach on routine obstetric ultrasound screening.

Methods: We searched our computer database over the previous decade for all cases in which this finding was described and reviewed the details of each case. We then cross-referenced with our local pediatric surgical unit and perinatal pathology department to obtain outcomes.

Results: We identified 84 cases. 24 had associated gastro-intestinal tract and respiratory anomalies; 22 had abnormal karyotypes (10 Trisomy 18s, 5 Trisomy 21s and 1 each of other aneuploidies or other karyotypical abnormalities); 6 had neuromuscular syndromes; 3 had major central nervous system anomalies; 7 had renal anomalies causing anhydramnios; 5 had other genetic syndromes; 2 had placental insufficiency leading to anhydramnios; 8 were found to have normal stomach appearances and had normal outcomes and 7 had a normal outcome despite persistently absent stomach on ultrasound examination.

Of these 84: 26 underwent termination of pregnancy; 9 suffered in utero fetal demise; 8 died in the neonatal period; 3 died in infancy; 44 had a live birth and survived infancy and 5 outcomes were not obtained.

Conclusions: A persistently absent stomach on ultrasound scanning is associated with a guarded prognosis – with an incidence of abnormal karyotype of 29% and a high incidence of associated structural abnormalities. In only 9.2% of persistently absent stomachs was the outcome normal. We have not been able to explain why these normal fetuses did not demonstrate stomach ‘bubbles’ on ultrasound.

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Musculoskeletal diseases in pregnancy

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Aim: The study and recording of the muscular diseases on the duration of pregnancy at pregnant that were attended by the obstetrical – gynecological clinic of hospital of Pyrgos.

Material and Method: There were studied pregnant at the years 2003 until 2008 with observation on every quarter of gestation and free background from musculoskeletal symptoms. On total of 2470 pregnancies we studied and record the musculoskeletal diseases analyzing cards of follow up, the childbirth background and the therapy.

Results: The pregnant reported one or more musculoskeletal symptoms usually at the second and third quarter of gestation. These symptoms were result of the weight increase, the spine lordosis because shift of weight, the fluid retention by tissues and joints, the calcium and magnesium disabsorption and the action of relaxine hormone. The most frequent muscular diseases are waist pain 64.5%, low back pain 61.4%, pain in the sacrum 55.6%, cramps 32.1%, pubic symphysis pain 29.6%, pain at the joint of forearm and carpus usually expresses as carpal canal syndrome 21.5%, rib pain 19.6%, pubic symphysis diastasis 1.5%.

The 80% of pregnant were faced conservatively from the obstetrician (appropriate information, analgetic medicines, diet, physical exercise, calcium and magnesium supplements) while the 20% were referred in orthopedist or even neurologist. Indications were the beginning of symptoms until the first quarter of gestation, the intensity and the frequency, the pennant’s wish, the failure of the conservative treatment and the appearance of neurologic symptomatology.

Conclusions: The diseases of the musculoskeletal system in pregnancy are frequent and they are corresponded at conservative therapy.

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Partial hydatidiform mole with klinefelter karyotype

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Introduction: Gestational trophoblastic disease forms a heterogeneous group of interrelated alterations characterized by an abnormal proliferation of trophoblastic epithelium. This broad spectrum of entities includes: complete hydatidiform mole, partial mole, gestational trophoblastic carcinoma and trophoblastic carcinoma of the implantation site. Although triploidy is the most likely karyotype, cases of normal karyotypes have been reported with phenotypically normal infants. In this poster we present a case of prenatally-diagnosed partial hydatidiform mole in which fetal karyotype showed a classic Klinefelter syndrome. We review the karyotypes of our molar pregnancy casuistry.

Case presentation: A thirty-three-year-old woman, light smoker with two previous eutocic deliveries was brought to Emergency Room at fourteen weeks of pregnancy complaining of resistant hyperemesis not responding to usual treatments, vaginal haemorrhage, anxiety and insomnia. An ultrasound examination showed one live fetus of thirteen weeks and five days, normal cardiac activity and movements. Placenta was implanted in the posterior uterine wall with a thickness of 6cm. Trophoblast appeared heterogeneous, with multiple vesicle-like images (fig. 1 and 2). Amniocentesis was performed disclosing a 47 XXY karyotype. Final diagnosis was classic Klinefelter syndrome.

Conclusion: The main conclusion is that, to our knowledge, this is the first reported case of the association of a partial hydatidiform mole with a live fetus with Klinefelter syndrome. This suggests that any genetic abnormality, aneuploidy, autosomic anomalies, even normal karyotype or sexual chromosome alterations may coexist with a trophoblastic disease identical to partial triploid mole. Finally, we perform a review of the genetics of our molar pregnancy casuistry.

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Temporary bony defect over maxilla detected at 2\textsuperscript{nd} trimester diagnosed as I-cell disease in the postnatal period

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Introduction: Inclusion-cell (I-cell) disease, also referred to as Mucolipidosis type II, is an inherited lysosomal storage disorder. It is an autosomal recessive disorder caused by an deficiency of GlcNAc phosphotransferase, which phosphorylates mannose residues to mannose-6-phosphate on N-linked glycoproteins in the Golgi apparatus within the cell. It presents as developmental delay, growth failure, rapid psychomotor deterioration, hip dislocations, inguinal hernias, hepatomegaly, joint limitation, and skin changes. Here we reported a case with temporary bony defect over maxilla detected at second trimester finally diagnosed as I-cell disease.

Case report: A 23 year-old women was referred to our department due to the suspect of fetal cleft lip. Detailed ultrasound was performed. Ventriculomegaly as atrium 9.33mm and a hole at maxilla were found. Otherwise, no other abnormalities were noted. Cleft lip was suspect at that time. The baby was born at 37 weeks' gestation with birth body weight 2105g via vaginal delivery. No cleft lip or palate were noted after birth. Marfan syndrome was initially diagnosed due to long limbs and coarse facial features. Frequent infection and recurrent apnea occurred during first year. With the baby development, shprintzon Goldberg craniosynpsis was noted. I-cell disease was finally diagnosed by enzyme analysis. The baby was died 1 year later due to severe infection.

Conclusion: Dysostosis multiplex is the characteristic pattern of skeletal abnormalities in I-cell disease. Prenatal skeletal defect is rarely reported. Temporary bony defect over maxilla may be the novel sign in prenatal diagnosis of I-cell disease.

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Case report: A case of congenital chylothorax with suspicion but not confirmed non compactatum myocardium

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Case report: a case of congenital chylothorax with suspicion but not confirmed non compactatum myocardium. Chylothorax is a rare disease that eventually progresses with non-immunological hydrops fetalis. We report a case of congenital chylothorax in a female fetus. In the second trimester we performed an anomaly scan and identified a relatively small cardiac area. The fetus developed after 7 weeks a small pleural effusion in the right side and mild polyhydramnios. Corticosteroids were prescribed for lung maturation. The fetal echocardiography showed left ventricular volume increased with crypts suggestive of non compactatum myocardium, preserved cardiac function and minimal pericardial effusion. Serial ultrasonograms were made. At 35 weeks and 3 days the fetus showed anasarca and severe polyhydramnios, and we decided to deliver. She was born with 3,360g and Apgar index of 4 and 7. At the first examination, the newborn had bilateral pleural effusion, hepatomegaly, ascites, jaundice, congestive heart failure and severe respiratory distress so it underwent to bilateral pleural drainage and maintained with mechanical ventilation showing good progress. With 35 days of life, the child replicated the pleural effusion, then she was submitted to a new thoracic drainage with output of milk appearance liquid. The biochemical analysis of pleural fluid showed the presence of 5800 leukocytes/mm³ (89% lymphocytes, 8% macrophages, neutrophils 3%) and triglycerides of 1470mg/dl, confirming the diagnosis of chylothorax.

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Prenatal diagnosis of campomelic dysplasia

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Campomelic dysplasia is a rare congenital skeletal condition characterized by abnormal development of bones and cartilage. In the majority of cases is associated with sex reversal of 46XY fetuses and is caused by a mutation in gene Sox9 (SRY-like high-mobility group) of chromosome 17. The transmission is autosomal dominant and the majority of carriers die during the fetal and early neonatal period from respiratory failure.

We report a case of prenatal diagnosis in the 20th week made by ultrasound findings with the characteristic shortening and bowing of the long bones of the lower limbs. Due to the bad prognosis of the disease, a decision of termination of pregnancy was taken at the 24th gestational week. Fetal pathological examination confirmed sonographic findings.

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Tetraploidy in a fetus with several ultrasound anomalies: A case report

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Introduction: Tetraploidy in humans is usually lethal, and fetuses found to have it are usually aborted at the first trimester and rarely proceed to birth. The incidence of tetraploidy is 2.0% to 3.2% in spontaneous abortions and 5% to 6% among abortions with chromosomal abnormalities. Nonmosaic tetraploidy may occur by (1) trispermic fertilization of a haploid ovum, (2) fertilization of a diploid ovum by a diploid sperm, (3) cytoplasmic cleavage failure at the first mitotic division of the fertilized ovum, or (4) fusion of 2 fertilized cells.

Case Report: A 35-year-old G3P2, Caucasian woman, without significant medical or family history, was referred to our unit because several ultrasound anomalies were detected at second trimester ultrasound. The parents were not consanguineous and the male partner was 28-year-old. The initial screening scan was performed at 12 weeks gestation with a normal nuchal translucency (1.8mm for a CRL of 64mm). At 20 weeks gestation, the ultrasound detected: hydrocephaly, myelomeningocele, cardiac anatomical anomaly (transposition of great vessels) and multicystic left kidney. Amniocentesis at 20 weeks gestation revealed a 92, XXY karyotype. The patient decided to interrupt the pregnancy at 22 weeks. Autopsy findings were consistent with those found in ultrasound examination.

Conclusion: In this case, the second trimester ultrasound was of great importance to allow timely diagnosis and interruption of pregnancy before 24 weeks gestation, which is the legal limit in Portugal. No additional genetic studies were performed and the cause of nonmosaic tetraploidy of the fetus is unknown.

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Prenatal diagnosis of short rib-polydactyly syndrome, Saldino-Noonan type at 12th gestation

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A case is described in which the ultrasonographic findings during the 12th gestational week led to the suspicion of a skeletal dysplasia and an abortion was induced. The ultrasound image disclosed extra fingers and toes, extremely short limbs, megacystitis and short ribs. The Pathological-anatomical examination confirmed the suspected skeletal dysplasia. The diagnosis was Short rib-polydactyly syndrome, Saldino-Noonan type. Typical skeletal changes, megacystitis, uretral atresia, short ribs and pulmonary hypoplasia, heart defects were espacially indicative of this syndrome. Most of the cases were diagnosed between 16th and 24th weeks of gestation. In this case we reported a very early diagnosed syndrome.

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Prenatal sonographic assessment and postnatal outcome in the various types of sacrococcygeal teratoma

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Objectives: 1. To evaluate sonographic findings according to the types of sacrococcygeal teratoma (SCT). 2. To analyze postnatal differences according to the types of SCT.

Method: Between March 1997 and February 2008, we identified 10 fetuses with SCT diagnosed antenatally and retrospectively reviewed the records of mothers and infants at Asan Medical Center. The sonographic findings were assigned as type I in 3 patients, type II in 3, type III in 2, and type IV in 2. Tumors consisting of both cystic and solid components were detected in 8 cases while an entirely cystic teratoma in 2 cases with type IV tumor. The mean diameter at delivery in type I, II, III, and IV tumors was 5.6cm, 11.6cm, 3cm and 8cm, respectively. Polyhydramnios was present in 2 cases with type II tumor. The mean gestational age at delivery was 38 weeks and 8 infants were delivered by caesarean section and 2 by vaginal delivery. Pathologic examination revealed mature teratoma in 8 cases and immature teratoma in 2 cases. The follow-up time ranges from one to seven years (mean 3.2 years). All of the infants are currently tumor-free but one with type II tumor has a urologic problem.

Conclusion: Although our data was statistically insignificant due to the small number of cases, the prenatal diagnosis of SCT by ultrasound was accurate and the prognosis of SCT was favorable.

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**Adnexal masses in pregnancy**

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Objectives: Unordinary appearance of gelationous cystis in pregnancy, and border line carcinoma ovarii in pregnancy.

Study Methods: We had 15 women with cystic tumors, larger than 50mm, in pregnancy. We made ultrasonography examinations and doppler study, tumor marker tests, sedimentation, leukocyte formula, and punction of cystic in cases with possible torquation and cytology, bacteriology and biochemistry analysis. The Results were analyzed by Fisher test.

Results: From 15 cases of cystic tumors over 50mm in pregnancy, be had 7 punctions in dimension from 120 to 250mm (approximately 50%), and no cytology or bacteriology pathology. Only the higher percentage of glucoses and proteins in the gelationus fluid. In all cases tumor markers are normal (Ca 125). Doppler flow of cystic capsula was from Ri 0.65 to 0.78. Doppler flow of ovarii was in optimal levels. In 5 cases (33.3%) we had the decrease of resistant index in cystic capsula by coming to the 38weeks of gestation, and largening of the tumors. It was significantly hige lavel (p<0.001). We decided to make the caesarean section and adnexectomy. In all operative finisher pregnancies we had border line carcinoma of ovarii (p<0.001). The treatment was finished by the operation.

Conclusions: We concluded that doppler flow is the most important factor in predictable diagnosis, and in all suspectious cases of growing adnexal tumors in pregnancy we have to be more precise. The malignant tumors are more frequent in our population.

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Desmoid tumor of the abdominal wall end pregnancy

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Introduction: Desmoid tumors are slow growing fibromatoses tumors which have potential of infiltration on the surrounding structures, but have no metastatic potential (1) The are benign myofibroblastic neoplasms originating from the muscle aponeurosis.

Case report: A 29-year-old patient her second pregnancy; her first pregnancy was with caesarean section. During her second pregnancy in the fourth month on the abdominal wall a formation as a size of a nut was recognized. During the regular check-ups besides the good development of the pregnancy an enlargement of the formation was also noted. By the end of the pregnancy the size of the tumor was 70x65mm. In her 38 gestational week it was scheduled for her caesarean section. After opening the front abdominal wall, under the fascia profunda and above the peritoneum, close under the right mm.recti abdominis, we came across the formation which was as big as a women’s fist. After caesarean sectio we called an abdominal surgent and with the same discretion it was removed.

HP analysis: The desmoid tumor is macroscopically composed of a well-defined capsule infiltrated by collagen network with fibrotic sections.

Discussion: Desmoid tumors are benign deep fibromatoses, originating from fascia and muscle aponeurosis with an infiltrating growth. The desmoid tumors are often associated with previous surgical trauma (2) Therefore the most effective treatment still is the resection with clear margins although it may not prevent local recurrence.


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Echocardiographic prenatal diagnosis of rhabdomyoma case presentation

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Background: Cardiac tumors are very rare in children, especially in neonatal period. Common tumor in this age is rhabdomyoma, usually is multiple, some time associated with tuberose sclerosis. Clinical manifestation depends from number of tumors, localization and size. The new echocardiographic methods make it possible early diagnosis, follow up and safe delivery.

Aim of presentation is presentation of the two cases with multiple rhabdomyoma, diagnosed in prenatal period.

In two fetuses (one in 32 weeks and one in 37 weeks) were diagnosed multiple rhabdomyoma. In the first fetus were registrated 7 tumors and one of them was located in OTLV with severe compromition of outlet flow. Fetus has developed dilatation of left ventricle and cardiac failure. Pregnancy was finished in 37 weeks but flow through OTLV was extremely low and child has died after 2 days. In the second case were registrated 9 tumors in different parts of heart but with good toleration and good heart function. Pregnancy was finished in term, naturally, and baby was without clinical cardiac signs. Following up child during 4 month we concluded that hi is still in good condition and tumors are decreasing in mass.

Conculsion: Echocardiographic methods are the valid method for prenatal diagnosis of cardiac tumors including morphological and hemodynamics disturbances caused from tumors.

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Clinical analysis of prenatal cytogenetic diagnoses: 
10-year experience at asan medical center

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Objective: To review and evaluate a total of 6474 cases of prenatal cytogenetic diagnoses at Asan Medical Center from 1999 to 2008.

Methods: We reviewed the medical records of the patients in whom the procedure for prenatal cytogenetic diagnosis was performed. A total of 4557 cases of amniocentesis, 1401 cases of cordocentesis, and 515 cases of chorionic villus sampling were analyzed. The cytogenetic Results, indications for prenatal cytogenetic diagnoses, maternal ages, and the profiles of abnormal karyotypes were reviewed. We calculated the positive predictive value of each indication for abnormal fetal karyotypes and evaluated a factor that was the most sensitive marker for abnormal fetal karyotypes.

Results: Among the 6474 cases of prenatal cytogenetic diagnoses, abnormal karyotypes were identified in a total of 366 cases (5.6%). The most frequent indication for prenatal cytogenetic diagnosis was abnormal maternal serum screening (33.9%), followed by ultrasonographic abnormality (22.9%) and old age (20.0%). No significant difference was found between mean maternal age with and without abnormal fetal karyotypes after excluding balanced rearrangements and polymorphisms (31.9±5.3 vs. 32.1±4.5 years). Among the 258 cases of abnormal fetal karyotypes after excluding balanced rearrangements and polymorphisms, the most frequent indication for prenatal cytogenetic diagnosis was ultrasonographic abnormality (58.7%), followed by abnormal maternal serum screening (10.9%). The positive predictive value of ultrasonographic abnormality for abnormal fetal karyotype was 9.9%.

Conclusion: Among the several indications for prenatal cytogenetic diagnosis, ultrasonographic abnormality could be the most predictive marker for abnormal fetal karyotypes.

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Ondine’s syndrome – an unusual case

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Background: Congenital central hypoventilation syndrome (CHHC) is a rare condition with an estimated incidence of 1 case per 200,000 live births (1). It is defined as the failure of automatic control of spontaneous respiration, in the absence of cardiopulmonary disease. Other subtle manifestations, in varying degrees - Resulting from autonomic nervous system dysfunction - may be present, such as gastroesophageal reflux, with poor swallowing, decreased intestinal motility, with constipation, decreased heart rate variability and blood pressure fluctuation (2-5). About 15-20% of patients with this hypoventilation may also have Hirschprung disease, named as Haddad syndrome (4). The underlying cause is thought to be an abnormality of neural crest development and/or migration (3); however, the exact pathophysiology of CHHS remains unknown (2). Testing for PHOX2B mutation can confirm the diagnosis (3).

Case report: 24 years-old pregnant women, G3P2, with no relevant past medical history. Interventricular communication and pulmonary stenosis diagnosed by the 21st week. Polyhydramnios and long periods of reduced baseline variability of the fetal heart rate were identified, which lead to labor induction on the 38th week. Post-natal persistent evidence of hypoventilation during sleep, with absence of primary pulmonary disease or neuromuscular dysfunction and no heart disease with hemodynamic repercussion was the condition for the search of the mutation of the gene PHOX2B.

Conclusion: However the onset of Ondine’s curse symptoms usually occur during the first year of life, some autonomic deregulations signs may be verified on the fetal period.

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Prenatal diagnosis, development and outcome of a fetus with V. Galeni malformation and consecutive intrauterine cerebral infarction

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First presentation of a healthy woman II/G/IP, 26 years, BMI 33.3, 10 cigarettes/d, no regular medication, no former operative interventions, one healthy child after unproblematic delivery at a tertiary referral center: 31st gestational week, intact singleton pregnancy. Sonographic assumption of an atypical unilateral ventriculomegaly with hydrocephalus on the right hand side. Consecutive displacement of frontal cerebral structures. Additionally sonographically dense structure adjacent to dilated areas of initially unknown origin. No further evidence of fetal or materno-fetal anomalies. TORCH negative. Amniocentesis: Normal karyotype, 46, XY. Serial ultrasound scans revealing non-progression of ventriculomegaly without displacement of falx cerebri.

Hospital admission at 38 gestational weeks for elective induction of labor. One day later regular delivery of a male newborn, 3015g, length 48cm, APGAR 7/8/9, UA-pH 7.42. Cutaneous venous malformation on the right side of face. Postpartal Ultrasound/C-MRI: Cerebral infarction and soft tissue defect parieto-occipital on the right side; expanded epidural haemorrhage; arterio-venous-V. Galeni malformation. No confirmation of hydrocephalus. No surgical intervention necessary. Normal clotting values/serological parameters, haemoglobin 194g/l. Second C-MRI two weeks later with no-change situation. Follow-up 2 months: child without neurological impairment, no impending intervention.

Conclusion: Capillary malformation-arteriovenous malformation (CM-AVM) is a rare hereditary disorder. Various capillary malformations may be the result of RASA1-gene defects which lead to abnormal angiogenic remodeling of the primary capillary plexus that cannot be compensated. Prenatal detection via ultrasound is feasible and enables proper perinatal management and scheduling of diagnostic procedures. Normal childbirth is possible. Birth should take place in a neonatologically well experienced perinatal centre.

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**Stuve Wiedemann syndrome – an algorithm for prenatal diagnosis**

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Introduction and objective: Congenital bowing of long bones presents diagnostic dilemma during prenatal scan. Stuve Wiedemann syndrome (SWS) is a rare autosomal recessive syndrome and mainly presents with camptomelia prenatally. Prenatal diagnosis has been reported rarely in cases of recurrent disease.

In this study, we are reporting our experience on this disorder and prenatal diagnosis in a fetus with negative family history utilizing the sonographic algorithm that we have developed from our experience. This algorithm helps to distinguish SWS from other bent bone disorders namely camptomelic, kyphomelic dysplasia, femoral hypoplasia-unusual facies, Antley-Bixler and cuming syndromes.

Materials and methods: We analyzed details of 7 fetuses seen in our fetal medicine unit, Tawam Hospital, Al Ain District, United Arab Emirates, over a period of 6 years from 2002-2008 with a confirmed postnatal diagnosis of SWS. Analysis was done retrospectively by reviewing the patient charts and ultrasound images. Biometry, all long bones, thoracic size, liquor volume and associated anomalies were studied.

Results: The main ultrasound findings were: mild micromelia, bowing mainly in lower limb, tibia more than the femur, with relative sparing of fibula and upper limb bones, normal thoracic dimensions, progressive development of growth restriction and few associated anomalies such as talipes and camptodactyly. In 3 fetuses, there was unexplained oligohydramnios but with normal Dopplers.

Conclusion: SWS is a very uncommon skeletal dysplasia that is rarely diagnosed prenatally. The introduced algorithm might assist in the prenatal diagnosis of SWS and will guide to required molecular studies.

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A newborn with “Arnold-Chiari Syndrome” diagnosed at 25 weeks – how to manage?

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Introduction: Arnold Chiari Syndrome is the most common serious malformation of the posterior fossa, with an incidence of 1 per 1,000 population and greater incidence in female s. It is associated with significant morbidity and mortality. In the first years of life, mortality rate achieves an overall 15% rate, increasing to a 50% overall rate by some authors. There are several complications associated with this malformation, which can impair development and life of the infant.

Case Report: A 19 years old woman, primipara, followed by a particular obstetrician, was sent to our prenatal diagnosis centre because of SNC malformations diagnosed at 25 weeks gestational age. A Arnold-Chiari type II syndrome was diagnosed, associated with myelomeningocelo and osteoarticular changes in the lower limbs. The pregnancy was followed in our high risk pregnancy department. The patient refused to do diagnostic amniocentesis despite counseling and pregnancy was closely followed in our hospital until 37 weeks gestational age. A scheduled caesarean section was performed, with a female newborn with 2,915g, Apgar 1st minute 5, 5th minute 8, with myelomeningocelo and morphological osteoarticular alterations of the lower limbs.

Discussion and conclusion: Despite the early detection of this congenital malformation, pregnancy achieved 37 week's and subsequent complications and morbidities associated with the newborn occurred. Should this cases known to have difficult evolution and bad prognosis be managed another way? We think that yes, there should be more intervention, so that the fathers could realize the importance of the decision of non interruption, if possible.

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Difficulties screening of fabry diseases

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Introduction: Deficiency of $\alpha$-galactosidase A Results in progressive intracellular accumulation of the cell membrane-derived glycolipid, globo triaosyl ceramide. Progressive accumulation of substrate is associated with a wide range of disease signs and symptoms, including renal failure, cardiovascular dysfunction, neuropathy, stroke and dermatological manifestations in the form of angio keratomas.

Methods: Traditional newborn screening focuses on disorders for which early treatment prevents severe morbidity and mortality.

Results: Recessive genes on the X chromosome have different consequences in males and females. A mutated recessive gene on the X chromosome tends to have little impact in a female because there is a second, normal, copy of the gene on the other X chromosome. By contrast, a mutated recessive X-linked gene will have an impact in a male because the genes on the Y chromosome are different from those on the X chromosome, and no second copy of the gene exists.

Discussion: The condition affects hemizygous males, as well as both heterozygous and homozygous females; males tend to experience the most severe clinical symptoms, while females vary from virtually no symptoms to those as serious as males.

Conclusion: Fabry disease is a rare, X-linked lysosomal storage disorder which Results from a deficiency of the enzyme $\alpha$-galactosidase A ($\alpha$-Gal A). Enzyme replacement therapy is not a cure, and must be infused recurrently for maximum benefit. The diagnosis of FD was confirmed by Results of enzymatic tests.

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Mosaic isochromosome 10p – a case report

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Background: Mosaic isochromosome 10p is a rare chromosomal abnormality, with only one case reported. The authors present a case of a mosaic 10p tetrasomy associated with an isochromosome and describe the corresponding phenotype.

Case report: A stillborn male was the product of a spontaneous pregnancy. The progenitors were non-consanguineous with normal karyotypes. The gestation was uneventful until the 21st week, when a routine sonogram revealed frontal bone narrowing, hydrops fetalis, cardiomegaly and clubfeet. The echocardiogram showed tricuspid insufficiency, mitral stenosis and heart failure. The karyotype on amniocytes revealed two cell lines: a normal male karyotype (86%) and another with a supernumerary chromosome (14%): mos 47,XY,+mar.ish i(10) p(10)(10PTELI006++)(7)/46,XY(43).

Further analysis with fluorescent in situ hybridization using subtelomeric probes confirmed the supernumerary chromosome to be an isochromosome from the short arm of chromosome 10(10PTELI006++).

The day after amniocentesis fetal death occurred and labor was induced with misoprostol, delivering a male fetus with 550g.

An intracardiac blood sample was obtained and revealed, as expected, a normal karyotype since isochromosomes show tissue specificity.

Conclusion: The tetrasomy 10p associated with the presence of an additional i(10p) is a very rare chromosomal abnormality. The present case has in common with trisomy 10p syndrome craniofacial anomalies and clubfeet. The only other similar case described besides the craniofacial abnormalities has severe arthrogryposis. Our case also displays cardiac involvement not usually described. Ultrasound and karyotyping are the tools to establish the definitive diagnosis.

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Importance of a widened genetic workup before attempting pleurodesis by OK-432 in fetal chylothorax: An insight inferred from a case of Noonan syndrome with PTPN11 mutation

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Fetuses with chylothorax are one of the very few diseases that can possibly be treated in utero. Thoracoamniotic shunting and pleurodesis are two major modalities of fetal therapy. We report a fetus of Noonan syndrome with a missense mutation c.182A>C (p.Asp61Ala) of PTPN11 gene who responded poorly to antenatal pleurodesis. Based on our previous publication and this case, we proposed that fetal chylothorax with genetic origin may be poor responders to antenatal sclerosing pleurodesis.

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Amniotic band syndrome: Report of a case with peculiar features

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Background: Amniotic band syndrome occurs in one every 1200 to 15000 births. In abortion pathology the incidence is even higher. The severity of the deformities that have been described are related to the timing of the amniotic rupture. Most of the cases are sporadic.

Case report: An 18years old woman in the 14 week of her first gestation was routinely screened by ultrasound. An abnormal wall defect located to the right of the umbilical cord was recognized. The gastroschisis allowed the protrusion of the small bowel. Additional findings were hydrocephaly, hypertelorism, cleft lip and palate and scoliosis. Chromosomal examination disclosed a 46XX karyotype. In an ultrasonography performed at 22-23 weeks no renal parenchyma or urinary bladder were observed.

Main outcome: Since it was a malformation incompatible with life, the pregnancy was interrupted. The product of gestation was thoroughly examined by the pathologist. The malformations described were confirmed. Additional findings were recognized, like an abnormal superior limb that originated close to the umbilical cord, abnormal facial clefts and abnormal brain morphology.

Conclusions: Prenatal diagnosis of amniotic band syndrome is possible by ultrasound during the second trimester. A previously unrecorded fetal anomaly of the upper limb is described.

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Cryptic subtelomeric deletion plus inverted duplication at chromosome 18q in a fetus with near-normal phenotype: Molecular delineation by multicolor banding

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Among aberrations involving chromosome 18, such as trisomy (or partial) 18, or deletion, complex rearrangement of chromosome 18 is rare. Reported cases often had partial deletion 18p and partial duplication 18q. These chromosome aberrations cannot be solved by conventional G banding, and tools like fluorescence in situ hybridization (FISH) or spectral karyotyping (SKY) are often necessary. In this report, we present a fetus with a complex 18q aberration that could not be completely delineated by a combination of G banding, subtelomere FISH, and SKY. The karyotype was finally solved by multicolor banding (mBAND).

A 31-year-old Taiwanese primigravida had normal antepartum examination since early pregnancy, except a unilateral choroid plexus cyst (CPC) detected by ultrasound at gestational age 20 weeks. Maternal serum Down syndrome screening (α-fetoprotein plus human chorionic gonadotropin) at 16th gestational week revealed a risk of 1/149, and therefore amniocentesis was performed at gestational age 21 weeks. Both parents had normal karyotypes. Conventional G-banding revealed additional material on 18q. SKY revealed a duplication involving 18q. However, subtelomeric FISH analysis showed further deletion of the subtelomeric region. Finally mBAND define the abnormality as invert duplication of the region 18q11.2 to 18q22. The karyotype was then 46, XY,der(18) del(18)(q22) dup(18)(q22q11.2) de novo. The parents decided to terminate the pregnancy at gestational age 25 weeks. We reported a unique complex cytogenetic abnormality involving chromosome 18q. Segmental inverted duplication of chromosome not only caused partial trisomy but also resulted in deletions. We demonstrated the feasibility of multicolor FISH banding (mBAND) to delineate submicroscopic chromosomal aberrations.

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Prenatal management of compound heterozygous 21-hydroxylase deficiency (CYP21A2) in a daughter of heterozygous carriers

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Father: 33 years old, oligozoospermia, turkish ancestry, mutation CYP21A2 Gln318X and gene duplication detectable (each event heterozygous)

Mother: 30 years old, primigravida, primipara, portuguese ancestry, mutation CYP21A2 Val281Leu heterozygous, conception by ICSI.

Fetus: Compound heterozygosity of the missense mutation Val281Leu (GTG>TTG) in exon 7 and the nonsense mutation Gln318X (CAG>TAG) in exon 8 of the CYP21A2 gene detected in amniocytes. The duplication of at least exons 1-8 of the father was also shown to be present in the fetus. It was not clear, whether the duplication involves the active gene or the pseudogene, i.e. whether the duplication is able to compensate for the loss of function conferred by the point mutation. Therefore, prophylactic 3x0.5mg dexamethason p.o. substitution was administered to the mother at 9 weeks of gestation in order to prevent malformations in the fetus.

Spontaneous birth at 38 weeks of gestation, birth weight 2420g, length 50cm, head circumference 32cm, Apgar 9/10/10, umbilical venous blood pH 7.26. Postpartal 17-hydroxy progesterone 18.7ng/ml; at 6 days 5.10ng/ml. Steroid profile and newborn screening unremarkable. Clinically no signs of virilization.

In this case, dexamethasone treatment was started as soon as the pregnancy was detected for security reasons. It was continued throughout the pregnancy, since at 10 weeks non-invasive genetic testing revealed the female sex of the fetus, and at 15 weeks genetic testing of amniocytes demonstrated compound heterozygosity in the fetus. After birth, no malformations were detected. Currently, a thorough steroid hormone follow up is being performed.

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An acardiac twin pregnancy managed to reach at term

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Introduction: Acardiac twinning (AT) is a rare anomaly affecting %1 of monochorionic pregnancies. It is characterized by a malformed fetus with an absent or a rudimentary heart. The head is commonly absent as are the upper limb structures but the central trunk is usually present. The high perinatal mortality of over %50 in the pump co-twin is mainly due to CHF or to prematurity induced by polyhydramnios. We present an AT case, managed to reach at term.

Case: A 29 years old G1 P0 patient referred with a suspicion of a placental mass at 24 weeks of pregnancy. US revealed a 24 weeks fetus with normal AFI and an anterior placenta with normal US features. On the right lateral wall, a mass of 42x 51mm in close proximity but separate from the placenta was observed. In follow up; the mass grew up and US revealed circulation within the mass. We observed bony structures resembling vertebra and femur but we couldn’t document any cardiac activity and accepted the case as an AT. At the 36th weeks the mass measured 131x81mm. The unaffected twin was normally developed up to 381/7 weeks of pregnancy. After delivery, the mass was 15x12cm. 820gr. Family declined autopsy due to insurance problems. Co twin is normal at birth and at she is one year of old without any medical problems.

Conclusion: AT is a rare event with a high mortality and morbidity rate. With the advances in perinatal medicine, it is possible to prolong the pregnancy even to term.

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Primary Pulmonary Hypoplasia – two case reports and review of literature

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We present two cases of primary pulmonary hypoplasia. They were not suspected antenatally. We then looked at the literature to see if there has been any progress regarding prenatal diagnosis of primary pulmonary hypoplasia.

In conclusion there has been some progress in the investigations prenatally but these need more studies to provide evidence.

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Our experience of prenatal DNA analysis in Duchenne/Becker muscular dystrophy

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Duchenne muscular dystrophy (DMD) and its allelic form Becker muscular dystrophy (BMD) are severe neuromuscular diseases both caused by mutations in gene encoding for cytoskeletal protein dystrophin. Inheritance is X-linked recessive, so affected parsons are males, while females are healthy carriers of mutations. The aim of this study was to estimate role of direct and indirect methods of DNA analysis in perinatal diagnosis of dystrophiopathies. Our study involved 11 unrelated families with at least one member affected with DMD or BMD. First step of analysis was detection of dystrophin gene deletions in probands, using multiplex PCR method. In families without gene deletions indirect gene analysis was performed by PCR amplification of three intragenic microsatellite markers. In 2 families prenatal DNA diagnosis on chorionic villi samples was done, only in male babies established by karyotype. In another 2 families early postnatal DNA analysis was performed. We detected dystrophin gene deletions in 6 of 11 unrelated probands. Prenatal diagnosis based on detected gene deletions showed: in one family two babies with deletions, indicating that they will be affected, and in another family healthy baby without deletion. Early postnatal DNA diagnosis confirmed affected brother in one family and two healthy cousins in another. Indirect DNA analysis was informative in 3 of 5 families without gene deletions, providing detection of carrier status in females. Early prenatal diagnosis based on DNA analysis of mutations is ultimate way of DMD/BMD prevention in affected families. Detection of female carriers is also important for genetic counseling.

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A probability model for noninvasive fetal anemia testing

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Objective: To evaluate a novel, non-invasive method to identify the risk of fetal anemia.

Materials and methods: A cohort of 124 isoimmunized pregnant women participated in the study. Blood flow velocities in middle cerebral artery (MCA) and inferior cava vein (ICV) were obtained with Doppler ultrasonography. Cardiofemoral index (CFI), obtained by the ratio between biventricular outer length and femur length, was performed at the first cordocentesis. CFI ≥0.60, peak systolic velocity in MCA ≥1.5 median multiples, and preload index ≥0.37 (ratio between blood flow velocities at atrial contraction and ventricular systole) were considered suggestive of fetal anemia. An ordinal logistic regression and a stage-based probability of fetal anemia were obtained according to ICV and blood flow velocities in MCA and ICV. The fetal hemoglobin concentration deficit was corrected for gestational age.

Results: Mean gestational age and mean fetal hemoglobin were respectively 27.98 weeks and 8.4g/dl. Among the 124 fetuses (91.9%) with anemia, it was moderate in 47 (37.8%) and severe in 51 (41.3%). Seventy percent presented abnormal CFI, whereas 47.6% presented abnormal blood flow velocities in IVC and 65.3% in MCA. The probability of severe anemia was 0.093% with 3 normal measurements and 77.19% with 3 abnormal measurements. With 2 abnormal measurements, this probability ranged from 22.67% (CFI and ICV) to 35.57% (CFI and MCA).

Conclusion: In pregnancies with high risk of fetal anemia, the noninvasive testing presented in this study provides reliable information regarding a stage-based probability of fetal anemia.

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Ischemia-modified albumin in pregnancy

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Objective: The aim of our study is to evaluate the physiology of Ischemia-modified albumin (IMA) in pregnancy and its rule in the prediction of pregnancies complicated by IUGR (intra-uterine growth restriction).

Methods: 87 women with singleton pregnancy followed in our centre were enrolled; to evaluate the differences between pregnant and non-pregnant levels of IMA, 198 normal women were enrolled as control. IMA assays were performed at 11-14 weeks (T1), 19-22 weeks (T2) and 3 hours after delivery (T3) on maternal venous blood.

Results: A significant and linear increase of IMA/normal albumin during pregnancy was found (Anova one-way, p<0.001) above all at 19-22 weeks (Levene test, p<0.01).

14 pregnancy were complicated by IUGR and 73 newborns were AGA; non-significant differences were found between two groups at T1 and T2, but a decreased value of IMA/albumin was found at T3 in our 14 cases (t-test, p<0.05).

Conclusions: Results of our study demonstrates that there is an increased IMA concentration during pregnancy compared with non pregnant women. This increase is linear and the highest values of IMA/albumin was found at the end of gestation (T3). This finding suggests that delivery could Result in an important oxidative stress condition.

Non-significant differences were found in T1 and T2 between IUGR and AGA groups. However, a decreased value of IMA/albumin in T3 was found.

It seems that mothers of fetus with IUGR are less exposed than the AGA ones to the oxidative-stress effects due to delivery.

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Poster session I: Screening procedures in perinatalogy

Biochemical screening and invasive technique in first quarter at PASSIR of Granollers
Pioneering test pilot in Catalonia

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Introduction: Prenatal diagnosis of fetal congenital anomalies is offered to all pregnant women in Catalonia, with no age limit: biochemical screening of maternal blood in first quarter (8-13 weeks) and second quarter (14-20 weeks).

Objective: To examine Results of biochemical screening for prenatal diagnosis of congenital fetal abnormalities in Granollers (Catalonia, Spain) during year 2008.

Methods: Setting. Community Program of the Sexual and Reproductive Women’s Attention (PASSIR) and Hospital of Granollers.

Design: A cross-sectional descriptive study.

Results: Biochemical screening in the first quarter was performed to 2115 pregnant women and in the second quarter to 233 women. In the first quarter 2066 women obtained low risk markers and 48 high risk for Down’s Syndrome. In the second quarter the Results were of low risk in 202 women and high risk in 27. There have been performed 68 chorionic villus sampling with the diagnoses of Down’s S (5), Edwards Syndrome (2) and others (1). In the ninety-seven amniocentesis performed all Results were of normality. There were no fetal losses caused by the technique.

Conclusions: The screening was performed to 2348 pregnant women. 0.34% of them had a fetus with congenital anomalies, with a 0.21% belonging to Down’s S. Invasive techniques were performed with no risk to pregnant women.

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Low 1st trimester PAPP-A: Association with intrauterine growth restriction

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Background: Recent data indicate that Pregnancy Associated Plasma Protein A (PAPP-A), a protein measured as a part of first trimester pregnancy screening, may be associated with adverse pregnancy outcome, such as intrauterine growth restriction (IUGR), small for gestational age (SGA) and premature birth.

Aim: To study the association of IUGR, SGA and premature birth with low 1st trimester PAPP-A and to establish a cutoff point.

Methods: Data of 232 live births were reviewed retrospectively for 1st trimester PAPP-A in association to IUGR, SGA and premature birth. IUGR fetuses were diagnosed using ultrasound criteria. SGA were considered neonates with a birth weight below the 5th percentile. PAPP-A MoM values <0.57 (10th percentile) and <0.45 (5th percentile) were considered as low.

Results: In 232 pregnancies with PAPP-A measurements 10 IUGR, 19 SGA and 19 preterm cases were identified. Median PAPP-A value was 0.93. In the IUGR group PAPP-A values were significantly lower (p=0.004) compared to those with normal pregnancy outcome. Out of the 232 pregnancies 46 had PAPP-A MoM values below 0.57 and 22 below 0.45. We found statistically significant differences in the prevalence of IUGR when 1st trimester PAPP-A MoM values were lower than 0.57 (p=0.01) and 0.45 (p=0.001). We did not find statistical difference in PAPP-A values in the premature birth (p=0.47) and SGA (p=0.22) group.

Conclusion: Low 1st trimester PAPP-A values (<0.45 MoM) is associated with increased IUGR prevalence. Further studies are required to investigate the role of PAPP-A protein in intrauterine growth restriction.

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Is there any correlation between first-trimester pregnancy-associated plasma protein-A (PAPP-A) and birth weight

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Objective: To evaluate the relationship between the first trimester maternal serum pregnancy-associated plasma protein-A (PAPP-A) and birth weight.

Materials and Methods: This study was a retrospective cohort of 524 pregnant women who underwent screening for fetal aneuploidy between 11-14 weeks of gestation and who delivered at our hospital. The correlation between the PAPP-A values and birth weights were investigated.

Results: There was not any significant positive or negative correlation between birth weight and PAPP-A levels (Spearman’s correlation coefficient r=0.074, p=0.093). Maternal serum levels of PAPP-A were similar in small-for-gestational age (SGA) and in control groups (0.81±0.54MoM vs. 0.99±0.63MoM, p=0.058), and in large-for-gestational age (LGA) and in control groups (1.15±0.59MoM vs. 0.97±0.63MoM, p=0.137). No association was detected between PAPP-A levels and SGA development [OR: 0.525 (95% CI: 0.272-1.014); p=0.055]. After the PAPP-A levels were divided into groups as <1.00MoM, 1.0-1.99MoM and >2.00MoM, the analysis showed that the PAPP-A levels have no association with SGA or LGA development (p>0.05).

Conclusion: Although PAPP-A is a marker of a placental function, according to our study the first-trimester PAPP-A is not correlated with the birth weight, on the contrary reported before in some papers.

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Vitamin K deficiency during perinatal period – especially liver maturation and Vitamin K procoagulant-inhibitor

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Coagulation-related plasma proteins develop slowly during the gestational period and are still markedly lower than normal at birth. Great interest exists in the status of the Vitamin K dependent procoagulation factors (Factor II, VII, IX and X) because a number of healthy newborns develop a postpartum bleeding tendency that is due to Vitamin K deficiency. Recently, it has become clear that Vitamin K dependent factors are produced which acts as competitive inhibitors with normal factors. The occurrence of such inhibitors, termed PIVKA (Protein induced Vitamin K antagonist), may conveniently be studied by simultaneously testing blood with the Normotest (NT) and Thrombotest (TT). In the presence of maximal amounts of PIVKA inhibitors the TT values are about half of those of NT values, and by calculating the ratio (NT-TT)/NT an approximate evaluation of inhibitors present may be obtained. Normally the ratio is close to zero, whereas in adequately anticoagulated patient the ratio 0.5 or over 0.5. NT, which indicates exogenous disturbance of blood coagulation, and TT, which indicates endogenous disturbance of blood coagulation, are prolonged in newborn infant especially LBW (Low-Birth-Weight) infants, while the existence of PIVKA could be proved only 4 cases out of 104 cases. This seems to suggest that the deficiency of blood coagulation factors in newborn infants depend on the production deficiency of coagulation factors due to the immaturity of the liver rather than the existence of inhibitors. An increase in ratio of NT-values might serve as an index of maturation of liver function in newborn infants, based on the significant correlation with gestational weeks.

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Sensitivity and specificity of OD650 for prediction of fetal lung maturity

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Background: Respiratory distress syndrome remains a common cause of neonatal morbidity and mortality. Consequently fetal lung maturity (FLM) testing plays an important role in establishing obstetrics management strategies.

Methods and materials:
This prospective study was performed on 80 pregnant women (between 28 to 40 weeks of gestation) and their neonates. The respiratory status of each newborn was evaluated standard clinical and radiographic criteria were used to diagnose RDS.

The ability of amniotic fluid optical density (OD 650) was evaluated by calculating the sensitivity and specificity of each value.

Result: Twenty (25%) infants developed RDS. OD 650nm more than 28% ratio predicted pulmonary maturity. Nineteen out of 20 RDS cases had been predicted correctly. The negative predictive value of OD 650nm >0.28 ratio was 97% and positive predictive value was 51% and the sensitivity for prediction of RDS was 95% and specificity was 70%.

Conclusion: measuring optical absorbance of amniotic fluid (OD 650) is a rapid simple and inexpensive procedure that compares favorably with other methods of fetal maturity assessment.

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Transplacental regulation of the renin-angiotensin system in offspring's kidneys

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The intrauterine environment influences kidney development and by lowering the number of glomeruli causes arterial hypertension later in life. Blockade of the renin-angiotensin system during development irreversibly harms kidney morphology. It was the purpose of the present study to clarify whether high salt intake in pregnancy affects the renin-angiotensin system in the developing kidney of the offspring. Sprague-Dawley rats were fed normal (0.15%), medium (1.3%), or high (8.0%) salt diets during pregnancy and weaning. The offspring were weaned at 4 weeks of age and subsequently switched to normal salt diet. Kidney morphology and blood pressure were assessed at 7 weeks postnatally as well as expression of components of the renin-angiotensin system in the offspring kidneys (by western blotting) at term and at 1 week of age. The final number of glomeruli in the offspring of the mothers on high salt diet (26545±6745) was significantly lower compared to the other groups (35525±7960). At term the expression of renin (69±32% vs. 100±18%), ACE (64±29% vs. 100±55%), and angiotensin II type 1 receptor (75±39% vs. 100±35) were significantly lower in the offspring of mothers on high-salt compared with other groups. On the contrary, at 1 week of age the expression of renin (134±34% vs. 100±25%) and angiotensin II type 1 receptor (131±64% vs. 100±46%) were significantly higher in the offspring of mothers on high-salt diet compared with the other groups. We conclude that high salt intake during pregnancy modulates the renin-angiotensin system in developing kidney leading to reduced nephron numbers in the offspring.

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Serum leptin concentration in healthy and infected full-term and preterm neonates

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Objectives: Suggestion that infections may change serum leptin concentration and modify intrauterine growth of fetus need more independent research.

Aims: 1) to evaluate the serum leptin concentration in healthy and infected newborns according to their maturity, sex, birth asphyxia and congenital infection. 2) to determine the correlation between leptin value and neonatal anthropometric parameters.

Material and methods: 146 (73 full-term and 73 preterm, 86 male and 60 female) newborns aged from 2nd to 4th day of life, among them 90 infected (36 with pneumonia, 30 septic, 7 with purulent meningitis, 14 with urinary tract infection) and 56 healthy. Serum leptin concentration in ng/ml were determined in venous blood using test IRMA (immunoradiometric assay, DSL, USA).

Results: Healthy (3,73 ± 1,49) and infected (3,94 ± 1,80) full-term newborns had statistically significantly (p<0.05) higher mean leptin concentrations than prematures (2,44 ± 0,35 and 2,44 ± 1,20). We found significant positive correlation between leptin value and GA in healthy (r=0.42) and in infected newborns (r=0.35), between leptin concentration and birth weight (r=0.42, r=0.42), leptin and length (r=0.42, 0.42 respectively), leptin and head circumferences (r=0.34, r=0.38), leptin and chest circumferences (r=0.40, r=0.39), both in healthy and in infected newborns. On the basis of multiply regression analysis we confirm the relation between leptin value and low Apgar score, female newborns, birth weight and GA.

Conclusion: Neonatal serum leptin concentration correlate with birth weight, gestational age, sex, general state after birth, length, head and chest circumferences in healthy and infected newborns. Intrauterine infection do not influence on the leptin concentrations in newborns.

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Fetal macrosomia – incidence and related risk factors

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Introduction: Fetal macrosomia represents a potentially harmful condition for mother and new born and difficult to predict with accuracy.
Objectives: We studied maternal risk factors, infant outcome and perinatal complications in such cases.
Methods: Fetal macrosomia was defined as birth weight =4000g or more. A retrospective hospital cohort study was carried out with a number of 665 macrosomic fetuses, between 2004-2008. Maternal variables (age, weight, pregestational physical activity, parity, diabetes, main caesarian section indication, meconium stained amniotic fluid) and perinatal variables birth injury, Apgar score at 1 and 5 minutes, need of intensive care, early mortality range were assessed.
Results: Incidence of fetal macrosomia was 4.48% with sex ratio male/female 2/1. Most cases of babies with macrosomia occurred in low risk pregnancies. Delivery mode was caesarian section in 369 (55.4%) cases and in 296. (44.5%) was spontaneous. We found perinatal complications more frequent in the group of diabetic fetal macrosomia and those with poor prenatal care. The leading cause of death -1 case- was asphyxia.
Conclusions: Most cases of babies with macrosomia occurred in low risk pregnancies. Vaginal delivery appears to be reasonable in cases of recurrent fetal macrosomia

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Optimising the provision of human milk for hospitalized sick newborn infants – recommendation for neonatal intensive care units

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Breastfeeding is the optimal method of infant feeding. The AAP extended its recommendation of breastfeeding to include premature and other high-risk infants either by direct breastfeeding or using expressed mother's milk.

We observe the low incidence and duration of breastfeeding among this high-risk populations. Most of sick infants can not be directly breastfed at birth. Potential institutional barriers include inadequate information regarding the benefits of mother's milk feeding for the infant, lack of consistence advice and support from health professionals and also difficulty securing appropriate equipment and supplies to express milk.

In light of evidence supporting the benefits of breastfeeding it is important to promote breastfeeding and minimalize barriers that may Result in early breastfeeding termination.

Mothers need to receive information describing the benefits of human milk for their infants along with the practical means to help them express breast milk until their baby is able to direct breastfeed. To increase the likelihood of transition to direct breastfeeding, health professionals need to provide support for long-term pumping as well as specific advice regarding the timing and progression to direct breastfeeding. Pumping should be initiated as soon as the mothers' condition permit and offering the opportunity to the mothers should be part of the supportive care offered by the postpartum staff.

Providing knowledgeable, accurate and consistent support should be the rule in perinatal center for mothers of high-risk infants who choose to breastfeed. The obstetrician and neonatologist should provide an appropriate rules of initiation and maintaining of lactation among these mothers.

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Urinary iodine levels and thyroid function tests of neonates and their mothers in aydin province

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Introduction: Iodine deficiency causes some developmental and functional diseases which can be prevented with iodine prophylaxis. According to WHO, TSH >5 mU/ml in more than 3% of the population and average urinary iodine levels <100 µg/L are defined iodine deficiency. We studied thyroid functions and urinary iodine levels in neonates and in their mothers in Aydin province.

Material and Method: Blood and urine samples were taken simultaneously from 400 newborns between 4-7 days of life and their mothers for determination of TSH, FT4, TT4 and TT3 and urinary iodine levels in provincial and district hospitals.

Results: Mean urinary iodine levels of neonates and mothers were 141.8±13.6, 128.8±12.4 µg/L, respectively. Mean of thyroid function tests was TSH; 7.26±7.87 (0.34-54.8)mU/ml, TT4; 13.9±3.6 (1.85-24) µg/dl, FT4; 1.68±0.33 (0.78-3)ng/dl, TT3; 187±60.4 (55-456)ng/dl in neonates and TSH; 1.71±1.35 (0.02-12)mU/ml, TT4; 12.9±2.37 (6.54-20.3) µg/dl, FT4; 1.29±0.22(0.52-2.22)ng/dl, TT3; 173.2±39.3(83-331)ng/dl in mothers. The ratio of neonates who are recalled back with TSH>9.1mU/ml was 22.5% and with TSH>5mU/ml was 47% and with congenital hypothyroidism frequency was 1.25%.

Conclusion: We obtained urinary iodine levels of neonates and mothers as normal. This situation shows the emphasis of iodinated salt usage by local health policies. The absence of iodine deficiency in those infants (47%) with high TSH levels make us think of other causes. Some other etiologic and physiopathologic mechanisms such as umbilical care with iodinated solutions, insufficient iodine intake in pregnancy and natural goitregens taken by the mother are thought to be effective in thyroid metabolism.

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The importance of the amniotic fluid glucose level (Polycentric Study)

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Aim: It is generally known that the mother’s glucose level can influence the fetus by causing a large
increase of its weight. The purpose of the present study is to investigate any possible relation
between the glucose level of the amniotic fluid and the weight of the fetus.

Material-Method: 56 women were in total included in the study. They underwent an artificial rupture of
the membrane during the natural birth and the amniotic fluid was collected in order to measure its
glucose concentration.

Results: The Results extracted from the biochemical control and the measurements of the birth
weight were the following:
a) Glucose level: <10mg/dl Average Birth Weight: 3361gr
b) Glucose level: 11-19mg/dl Average Birth Weight: 3256gr
c) Glucose level: >200mg/dl Average Birth Weight: 2969gr

Conclusions: 1) It becomes, therefore, evident that an inversely proportional relation exists between
the glucose level of the amniotic fluid and the birth weight of the fetus. A possible explanation could
be that the fetus, unable to use the glucose, eliminates it through its urine, which consists part of the
amniotic fluid and as a Result, the increased glucose level in the amniotic fluid corresponds to
decreased birth weight. 2) Consequently, it should be underlined that this measurement could be a
very useful indicator in certain cases, playing an important role for the prognosis.

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Fetal body in gestational diabetes

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Objective: 1- To assess the value of fetal body measurement in GDM patients on insulin.
2- To determine the outcome of pregnancies in mothers with GDM on insulin followed in the Fetal Endocrine Clinic.

Subjects & Methods: Forty nine pregnant women diagnosed with GDM and require insulin for glycemic control were prospectively followed at, specialized Fetal Endocrine Clinic (FEC). Patients had an anomaly scan at 24 weeks gestation. This is followed by a growth scan at 28-32 weeks, 33-36 weeks and a final scan at 37-40 weeks gestation. In each visit sonographic measurement of fetal biometry, estimated fetal weight, placenta thickness, amniotic fluid deepest pool, liver length, abdominal wall subcutaneous fat thickness and interventricular septum thickness.

Results: A total of 49 patients. Mean age was 35±6.2 years, mean parity was 3.9±2.9, the mean GA at first visit was 27±4.3 weeks. The mean booking BMI was 34.1±7.7. Forty three (87.8%) patients had a family history of diabetes and 42 (85.7%) had a history of GDM. Fetal growth and body measurements were within normal values. The mean GA at delivery was 39.2±1.3 weeks. Labor was induced in 12 (25%) patients. Fifteen (30%) patients were delivered by Caesarean section. The mean birth weight was 3388±531g. Only one (2%) neonate required admission to NICU.

Conclusion: Fetal body measurements during pregnancy correlate well with pregnancy outcome. Pregnancy outcome in patients with GDM on insulin could be as good as non GDM patients when followed in specialized maternal and fetal clinics.

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Treatment of persistent hyperinsulinemic hypoglicemia of the neonate

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Introduction: Persistent hyperinsulinemic hypoglicemia of the neonate is a rare heterogenous disease which is characterized by inadequately high insulin rates in the presence of severe hypoglicemia.

Aim: Efficacy of Octreotide in treatment of persistent hypoglycemia.


Clinically findings: normal except for systolic murmur at heart base, grade II/III and moderate hypotonia.

Echocardiography: Concentric hypertrophy of both chambers and of the cardiac septum. Hypoglicemia, confirmed on several occasions (0.6 mmol/L), resolved with parenteral glucose (up to 16 mg/kg/min), with formula diet given. Insulinemia during hypoglycemia was 20.2 mU/ml, and C-peptide concentration 2.23 nmol/L, with suppressed ketogenesis.

Results: As the findings indicated hyperinsulinemia, on the 13th day the child was introduced to therapy with Octretotide (100-150 µg daily 4 equal dosages), iv. application of glucose and adequate peroral nutrition. Regular glycemia check-ups. Adverse effects of Octreotide were not noticed. At age 3 months the child was discharged from hospital while glycemia were under good control with Octreotide in 2 dosages. (EEG, ECHO and endocranial CT were normal). According to Brunet-Lezine developmental scale at age 3 months the child matched age 2 months 21 days (IQ 90).

Conclusion: Octreotide has proved to be effective therapy for this patient with persistent hypoglycemia.

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Maternal risk factors for intrapair birth weight discordance in Japanese dichorionic twins

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Objective: We investigated the maternal risk factors for intrapair birth weight discordance in Japanese dichorionic twins.

Methods: A retrospective, hospital-based cohort study was performed with dichorionic twins with two live births managed at our hospital from 2003 to 2008. Twins were classified as discordant if there was a 20% or more weight discordance. Statistical differences between discordant and concordant twins were evaluated by chi-square test or Fisher’s exact test for categorical variables, and Student’s t-test or Mann-Whitney U-test for continuous variables, and logistic regression. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Differences of P<0.05 were considered significant.

Results: Of total 340 twin pairs, 56 were discordant and 284 were concordant twins. Forty-one were 20-29% discordant, nine were 30-39% discordant, and six were ≥40% discordant. Discordant twins were more likely to have maternal smoking (12.5% versus 4.2%, OR 3.23, 95%CI 1.21, 8.63, P<0.05) and to be associated with pregnancy induced hypertension (PIH) (32.1% versus 9.8%, OR 4.33, 95%CI 2.18, 8.57, P<0.001). No difference was seen for maternal age, parity, physique, gestational diabetes mellitus, history of infertility and in vitro fertilization. The logistic regression identified maternal smoking (adjusted OR 4.69, 95%CI 1.61, 13.6, P<0.01) and PIH (adjusted OR 4.54, 95%CI 2.25, 9.19, P<0.001) as great risks for discordant twins.

Conclusions: Maternal smoking and hypertensive disorders were associated with intrapair birth weight discordance in Japanese dichorionic twins.

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Ketoacidosis in GDM complicated pregnancies

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Ketoacidosis is a metabolic emergency which can affect both the lives of the mother and the fetus. It is the most dangerous complication which can occur in diabetic pregnancies, in spite of its incidence of only 1 percent. The fetal loss is of 20 percent.

Most of the times it is caused by medical problems, such as infections (pneumonia, virosis, acute gastroenteritis), hyperemesis gravidarum or diabetic gangrene. The rest of the triggers are: the discontinuation of the insulinotherapy, the use of corticosteroids for the fetal pulmonary maturation or beta-sympatomimetic agents for acute tocolisis in case of preterm labor, dietary mistakes. Any of these can cause hyperglycemia and glycosuria, therefore osmotic diuresis, which takes to plasma hyperosmolarity, together with sodium and kalium loss. The insulin deficit causes lipolisis, with the mobilization of fatty acids from the adipose tissue. After hepatic oxidation, these become ketonic corpes (beta-OH butyric acid, acetoacetic acid and acetone), thus causing metabolic acidosis.

The clinical presentation of ketoacidosis consists of symptoms such as: abdominal pain, nausea, vomit, polydipsia, polyuria, hypotension, acidic respiration, mental deterioration or even coma.

The laboratory findings include hyperglycemia over 300mg/dl, metabolic acidosis (ph<7.20, HCO3<10mEq/L), ketonemia and ketonuria. The treatment of ketoacidosis consists of iv use of insulin, rehydration, sodium and kalium supplementation, the correction of acidosis using alkaline solutions.

We present ours experience of treatment and the Result of 12 pregnancy complicated with ketoacidosis.

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**Biotinidase deficiency as problem for diagnostics in pediatrics and neonatology**

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Introduction: Younger children with profound biotinidase deficiency usually exhibit neurologic abnormalities including seizures, hypotonia, ataxia, developmental delay, vision problems, hearing loss, and cutaneous abnormalities.

Methods: Newborn screening for biotinidase deficiency (BD) provides prevention of neurological sequelae in patients with low residual enzyme activity by early treatment with oral biotin substitution. Two patients with biotinidase deficiency had diagnoses of infantile spasms made at one month of age. Biotinidase deficiency may be seen early in the neonatal period without the characteristic findings such as alopecia and seborrheic dermatitis.

Results: Evaluation of clinical and neuropsychological outcome showed that only patients with a biotinidase activity <1% exhibited characteristic clinical symptoms within the first weeks of life, while some patients with a residual activity of 1.5-5.0% did not develop clinical symptoms even when not treated until 19 years. The specific activities of propionyl CoA carboxylase, 3-methylcrotonyl CoA carboxylase and pyruvate carboxylase were found to be low in skin fibroblasts cultured in the absence of added biotin.

Discussion: Some children with biotinidase deficiency manifest only a single symptom, whereas others exhibit multiple neurologic and cutaneous findings. The isoform patterns of children identified by newborn screening are not different from those of symptomatic children.

Conclusion: All symptomatic children with profound biotinidase deficiency improve when treated with oral biotin. In epileptics this may be related to competition between biotin and anticonvulsants bearing carbamide ring for absorption. Biotinidase is the only enzyme that can cleave biocytin, a product of the proteolytic digestion of holocarboxylases.

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Congenital Methemoglobinemia in a newborn – a case report

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Cyanosis is a physical finding with multiple causes, e.g. neonatal sepsis, cyanotic congenital heart disease and airway abnormalities, or by abnormal forms of hemoglobin, as hemoglobin M. Methemoglobin results from oxidation of the hemoglobin molecule from the normal ferrous (Fe+2) to the ferric (Fe+3) state, Resulting in reduced oxygen binding and thus diminishing the oxygen-carrying capacity of blood and oxygen delivery to the tissues. Low levels of methemoglobin are maintained at 1% or less, by enzyme systems within the red blood cell. Increased levels of methemoglobin can occur due to congenital red blood cell abnormalities, or exposure to a high concentration of an oxidant substance.

We present a neonate with central cyanosis as a Result of congenital deficiency of the reduced nicotinamide adenine dinucleotide-cytochrome b5 reductase enzyme. The neonate was born at 36 weeks gestation, by vaginal delivery. Her birth weight was 2100g and Apgar scores were normal. The neonate was admitted to NICU after birth, due to cyanosis and tremor. Sepsis, structural congenital heart disease, prenatal administration and ingestion of oxidant dyes were excluded as a cause of the cyanosis, by history and appropriate tests. Hemoglobin electrophoresis was normal. Before treatment, methHb was 33g/dl. She responded very well to daily ascorbic acid administration, while her methHb levels normalized within two weeks. Daily dose of Vitamin C was 400mg/kg and Vitamin C levels were kept within normal limits. Since then, she has normal growth and development.

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Energy balance triangle in term newborns with intrauterine growth retardation (IUGR)

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Thermal, glycemic stability and establishing of normal breathing are key physiological functions making neonatological energetic triangle in children with low body mass in transitory period of metabolic adaptation, which includes the first 6-10 h after birth. Pathological variants - hypothermia, hypoglycemia and hypoxia - 3 H make pathological variant of energetic triangle and substantially affect their morbidity and mortality (1, 2).

Review of frequency of the most common pathological conditions in term newborns with IUGD, with special view to analysis of influences of hypothermia on hypoglycemia and perinatal asphyxia as pathological entities, pathological variants of energetic triangle

Study included 143 term newborns with IUGR admitted to neonatology ward at the Clinic Narodni front, Belgrade. Newborns were divided into two groups: with hypothermia - observed group, without hypothermia - control group. Selection analysis according to sex, gestation and body mass was conducted as well as comparative analysis of frequency of pathological states characteristic for IUGR depending on presence of hypothermia. Analysis was conducted by statistic tests of analytic and descriptive statistics.

There were 93 newborns in observed group and 50 in the control one. Analyzing sex, frequency of male gender in the whole group was 55.94%, and frequency of female gender 44.06% (p>0.05). In observed group average gestation was ?: 39.0, in the control one ?: 39.6 (p<0.01). Average birth body mass in the whole group was ?: 2,339g, in the observed one ?: 2,214g, and in the control one ?: 2,571g. Frequency of hypoglycemia in observed group was 53.8%, in the control one 24% (p<0.01). In the observed group frequency of pH<7.25 was 38.71%, and in the control one 14% (p<0.05). Mean value of Apgar score in the fifth minute in observed group was ?: 7.17, and in the control one ?: 8.12 (p<0.05). 38.71% of the observed group had 4-7 Apgar score, 10% (p<0.01) of the control one.

Hypothermia is one of the most basic factors of neonatal energetic triangle in the period of metabolic adaptation of newborns in the first 6-10 h of life, which is not simple time interval but has high share in morbidity structure of our tested newborns

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Liver metabolic diseases in infants and younger children – transplantation as therapy of choice

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Introduction: Hepatic transplantation for metabolic or genetic diseases of the liver produces a definite cure of the liver disease. Jaundice (icterus), the most visible sign of liver and biliary tract disease, is a condition characterized by yellow discoloration of the skin, sclerae, and mucous membranes as a Result of an elevated serum bilirubin concentration.

Methods: Laboratory-based and translational research has greatly increased our understanding of inherited metabolic liver disease. Specific diagnosis will usually depend on selecting laboratory tests in a logical manner, having defined the phenotype and considered the potential metabolic causes.

Results: Fourteen cases of metabolic liver diseases treated in this way have been reported, with excellent outcome. The diagnosis and therapy of the kids with metabolic liver disease is discussed, with an emphasis on maintaining quality-of-life and balancing the importance of early intervention with the stigmatization of the diagnosis of potentially life-threatening liver disease.

Discussion: Inborn errors of metabolism encompass a vast variety of disorders with myriad presentations and complex pathophysiology. Patients who present in the neonatal period have a poor prognosis. Immediate treatment is based on removal of toxic metabolites with dialysis.

Conclusion: Liver transplantation for inborn errors of metabolism not only replaces the diseased organ, but also leads to complete reversal of the metabolic defect. Until the promise of specific gene or enzyme replacement therapy is realized, liver and hepatocyte transplantation offers the best chance of achieving metabolic control in these challenging patients.

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Neuroprotective effects of melatonin upon the offspring cerebellar cortex in the rat model of BCNU-induced cortical dysplasia

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Cortical dysplasia is a malformation characterized by defects in proliferation, migration and maturation. This study was designed to evaluate the alterations in offspring rat cerebellum induced by maternal exposure to BCNU and to investigate the effects of exogenous melatonin upon cerebellar BCNU-induced cortical dysplasia, using histological and biochemical analyzes. Pregnant Wistar rats were assigned to five groups: intact-control, saline-control, melatonin-treated, BCNU-exposed and BCNU-exposed plus melatonin. Rats were exposed to BCNU on embryonic day 15 and melatonin was given every day until delivery. Immuno/histochemistry and electron microscopy were carried out on the cerebellum, and cerebellar tissue malondialdehyde (MDA) and superoxide dismutase (SOD) levels were determined. Histopathologically, normal developmental findings were observed in the cerebellae from the control groups. The maturation was delayed and the findings consistent with the early embryonic development were noted in BCNU-exposed cortical dysplasia group. There was a marked increase in the number of TUNEL (+) and Nestin (+) cells in BCNU-exposed group, but a decreased immunoreactivity to GFAP, synaptophysin and TGF was observed, indicating a delayed maturation, and melatonin significantly reversed these changes. Tissue MDA levels in BCNU-exposed group were higher than those in the control groups and melatonin+BCNU group (P<0.01), while there were no significant differences in the tissue SOD levels. These data suggest that exposure to BCNU on pregnant rats leads to delayed maturation of offspring cerebellum and melatonin protects the cerebellum against the effects of BCNU. Further studies are warranted to evaluate the mechanism of neuroprotective effect of melatonin administration during pregnancy on developing rat cerebellum.

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BDNF (Brain-Derived Neurotrophic Factor) and first trimester of pregnancy in humans

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Growing and renewing interest is been arising in the field of neurotrophins, in particular BDNF, in the last five years. However, there are no studies available in the literature nowadays regarding the possible interactions between the complex hormonal background of human pregnancy and this neurotrophin. On these bases, we decided to study the variations of its plasma levels in the first trimester of pregnancy in a group of healthy women (n=80), comparing them with those of a group of an healthy non pregnant control (n=73). Surprisingly we observed higher level of plasma levels of BDNF in control group rather than in group in pregnant women at first trimester (control: 836.397±17.7957 vs. pregnant at first trimester: 692.243±42.2254; p<0.01), with no differences in terms of BMI and age. However, on the basis of the paucity of the data present in literature and of those obtained in our protocol study, we can not establish which is the main mechanism by which BDNF plasma level seems to be reduced in the first trimester of human pregnancy. We can hypotize that this reduction could be related to some clinical aspects of neurovegetative disorders observed in first trimester and that BDNF could have a role in the physiological development of pregnancy. For this, more studies are needed to investigate these and other unanswered questions about BDNF and human pregnancy.

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Wnt signalling key effectors differ in embryo brain following intrauterine hypoxia-ischemia brain damage and reperfusion

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Objective: Wnt-signalling pathway has pivotal roles during the development of embryo brain. Recent studies have implicated a role for the canonical Wnt/beta-catenin signal transduction in rat hypoxic-ischemia preconditioned myocardium. This study investigated the relationship between Wnt-signalling pathway and intrauterine hypoxia-ischemia brain damage (HIBD).

Methods: We used a transient intrauterine model as embryo HIBD in gestational rat (17days). The rats were randomly divided into two groups. For transient intrauterine ischemia group, the gestational rat’s bilateral uterine arteries were occluded for 30 min, followed by reperfusion. For sham operation group, animals were subjected to the same surgical procedures without occlusion. Embryo brain samples were collected at 24, 48, and 72 h during reperfusion. Nissl staining and Caspase-3 immunohistochemical staining were performed to observe neuronal damages at hippocampus in each group. Western blot analysis was used to evaluate the expression levels of Dvl2, GSK-3beta, beta-catenin and LEF1.

Results: Results of Nissl staining and Caspase-3 immunohistochemical staining confirmed that transient intrauterine hypoxia-ischemia significantly induced neuronal apoptosis. The difference of beta-catenin expression level was no statistical significance between two groups. However, the level of Dvl2 and LEF1 both decreased while the level of GSK-3beta increased in transient intrauterine ischemia group.

Conclusion: This study provides preliminary evidence that the Wnt signalling may be repressed in intrauterine hypoxia-ischemia brain damage without the canonical Wnt/beta-catenin pathway, suggesting that the further research of the non-canonical Wnt/Ca2+ or Wnt/polarity signalling may contribute to a better understanding of Wnt signalling’s effect on HIBD.

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Investigation of maternal melatonin effect on the hippocampal formation of newborn rat model of intrauterine cortical dysplasia

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Cortical dysplasia is a cortical malformation resulting from any developmental defect during different periods of development. This study aims to contribute to the scientific literature by investigating the cerebellar histopathological alterations in neonates with cortical dysplasia due to the prenatal exposure to carmustine and the possible effects of prophylaxis with melatonin, a neuroprotective agent. Wistar albino female rats (200-220g) were randomly divided into five experimental groups; intact-control, sham-operated, exogeneous melatonin-treated, carmustine-treated and Carmustine+Melatonin-treated. Light microscopy, immunohistochemistry were carried out on the newborn hippocampus. Histopathology of hippocampus from the control, sham-operated and melatonin-treated groups showed continuity of migration and maturation which is a patognomonic sign of the newborn hippocampus. Carmustine group had cortical dysplasia and carmustine+melatonine group had brain morphology close to control group. However, hippocampal cortex from the newborn rats of cortical dysplasia group showed the histology of early embrionic hippocampal formation. Furthermore, immunohistochemically the increased apoptotic cell numbers and Nestin (+) cell numbers and the decreased positive immunoreactivity to GFAP, synaptophysin and TGF-β1 in the carmustine-treated group revealed a significant delay in brain maturation. It has been concluded that for women who need an alkylating agent treatment during their pregnancy careful ultrasound evaluation of fetal brain development is necessary and medical abortus indication must be kept in mind. Additional trials are required to evaluate the positive effects of prophylactic melatonin administration together with alkylating agent therapy during pregnancy.

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Senescence of fetal endothelial progenitor cells in pregnancies complicated by idiopathic fetal growth restriction

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Objective: The aim of this study was to investigate the number and functional ability of fetal endothelial progenitor cells in pregnancies complicated by idiopathic fetal growth restriction (FGR). Study Design: Fetal endothelial progenitor cells were isolated, and counted from 15 women with FGR and 30 normal women. Colony-forming assay and differentiation time assay were performed to detect functional activity of the cells. To assess cellular senescence, senescence-associated β-galactosidase staining was performed for endothelial progenitor cells. For quantitative analyzes of telomerase activity, the telomeric repeat amplification protocol (TRAP) assay was performed. Results: Compared with normal pregnancy, the number of endothelial progenitor cells was significantly lower, differentiation time from endothelial progenitor cell into outgrowing cell was longer, and the number of colonies after differentiation was smaller in FGR (p<.001), respectively. The intensity of senescence-associated β-galactosidase staining was higher in FGR (p<.001). The activity of telomerase was significantly lower in FGR (p<.001). Conclusion: The number and functional ability of fetal endothelial progenitor cells from FGR were significantly decreased and they were more senescent compared with those of normal pregnancy.

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Differential expression of cellular prion protein in the placetas of women with normal and preeclamptic pregnancies

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Objective: The aim of our study was to determine the difference of cellular prion protein (PrP\textsuperscript{C}) expression in the placetas of women with normal and preeclamptic pregnancies.

Methods: Placental tissues from 15 women with severe pre-eclampsia and 17 gestational age-matched normotensive women were collected at the time of their caesarean section. Quantitative reverse transcription polymerase chain reaction (RT-PCR), western blot analysis, and immunohistochemical staining were performed for mRNA expression, quantification, and tissue localization of PrP\textsuperscript{C} in each placenta.

Results: Compared with the normal placetas, PrP\textsuperscript{C} showed higher mRNA and protein expression levels in preeclamptic placenta (each, p<0.001). In immunohistochemical staining, PrP\textsuperscript{C} was present in the syncytiotrophoblast, cytotrophoblast, endothelial cell, and Hofbauer cell of villi of all placetas. These cells in normal placenta were week positive for PrP\textsuperscript{C}, and there was no difference of expression between each cell. In preeclamptic placenta, the PrP\textsuperscript{C} immunoreactivity of syncytiotrophoblast was higher than the other cells. When the PrP\textsuperscript{C} immunoreactivity in each cell was compared between normal and preeclamptic placetas, the syncytiotrophoblast was higher positive in preeclamptic placenta (p<0.001), but the other cells had no difference.

Conclusions: The increased expression of PrP\textsuperscript{C} in preeclamptic placenta may be a compensatory phenomenon for preeclampsia-related conditions. Furthermore, this change in preeclamptic pregnancy may give an explanation for placental response to overcome the preeclamptic conditions.

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Mutation analysis of the heme-oxygenase-1 gene in pre-eclampsia patients with a family history of hypertension in pregnancy

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Heme oxygenase (HO) is the rate-limiting enzyme in the degradation of heme to biliverdin. It is important for placental angiogenesis and the utero-placental hemodynamic control. Recently, it was demonstrated that HO-1 reduces the release of soluble Endoglin (sEng) and soluble Flt-1 (sFlt-1) which are both elevated in the serum of women with pre-eclampsia, from endothelial cells and pre-eclamptic placental villous explants. A possible regulatory function of HO-1 in the pathogenesis of pre-eclampsia can therefore be assumed. As pre-eclamptic disorders have a clear genetic component we performed a mutation analysis of the HO-1 gene in pre-eclampsia patients with a family history of hypertension in pregnancy. In 38 index patients, the promoter region, the whole coding region and the intron/exon boundaries of the HO-1 gene were screened for mutations by direct sequencing. No pathogenic variants were detected but we observed seven single nucleotide polymorphisms. The polymorphism -156T>C had not been described before. Like the well described (GT)n dinucleotide repeat and the SNP –413A>T this novel polymorphism is located in the promoter region of the HO-1 gene. The nucleotide exchange 99G>C was the only variant observed in the coding region leading to an amino acid exchange of Histidine for Aspartate. The other polymorphisms we observed were intronic. Allelic frequencies in pre-eclampsia patients were not significantly different compared to healthy controls for any of the polymorphisms. Based on our Results we conclude that variants in the HO-1 gene do not play a significant role in the pathogenesis of pre-eclampsia.

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Overperfusion-related retinal findings in pre-eclampsia: 
New insights regarding the pathophysiology of endothelial damage

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Background: Although retinal vasospasm is historically considered the main retinal finding in preeclampsia, a wide range of retinal findings is recognized in this condition. They are originated from choroid, which presents high susceptibility of overperfusion-related endothelial damage. Focal chroidal infarcts (FCI), characterized ophthalmoscopically by subretinal white spots and retinal elevation, are especially relevant in preeclampsia. The purpose of this study was to establish the main predictors of FCI.

Methods: Ninety-eight women with severe preeclampsia were submitted to retinographic documentation. An orbital color Doppler with a 7.5 MHz linear transducer provided ophthalmic artery resistive index (OARI) and ophthalmic artery mean velocity (OAMV). The association between retinal findings with OARI, OAMV, mean blood pressure at admission (MBPA), mean blood pressure elevation (MBPE), LDH and 24 hour proteinuria were obtained by fitted binary logistic models, established with variables categorized according to cutoff points obtained from ROC curves.

Results: FCI occurred in 46 (47%) women. Those with and without FCI presented significant differences in OARI (p<0.001), OAMV (p<0.001), MBPA (p<0.001), MBPE (p<0.001), LDH (p<0.001), and 24 hour proteinuria (p=0.005). The larger area under ROC curve was obtained with OARI (0.82±0.03), with the cutoff point of 0.56. The multivariate logistic regression model was obtained with OARI and MBPA, with odds ratio estimates of 7.10 and 5.29.

Conclusion: OARI is the major predictor of FCI in preeclampsia. Data support FCI as an overperfusion-related retinal finding secondary to endothelial damage in preeclampsia.

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Excess level of soluble fms-tyrosine kinase (sFlt-1) may be associated with pre-eclampsia in pregnancy with abnormal uterine artery Doppler during second trimester

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Objective: Preeclampsia (PE) has been proposed to be a condition characterized by an anti-angiogenic state, initiated by placental hypoxia. This cohort study aims to analyze the plasma concentration of sFlt-1 from pregnant women who present bilateral notching in uterine arteries Doppler in their second trimester. Methods: Thirty-seven non gemelar pregnant women at second trimester were selected and followed until delivery. Abnormal uterine arteries Doppler was defined as persistent bilateral notching after 26 weeks of gestational age. In women presenting this criteria, sFlt-1 concentration were determined with Quantikine (R&D Systems). PE was diagnosed based on gestational hypertension and proteinuria, according to NHBPEP Report (2000).

Results: PE occurred in 32.4% (12/37) pregnant women. Mean arterial pressure in these women was 123.3mmhg +/- 4.1. At delivery, mean gestational age was 37.6 +/- 2.9 weeks. Among women who developed preeclampsia, 45% (9/12) had bilateral notching in uterine arteries. Pregnant women who developed PE presented median sFlt-1 higher than with normal pregnancy (400.5pg/ml and 250.6pg/ml, respectively, p=0.01). Conclusion: Pregnant women with abnormal placental blood flow could be better followed with the inclusion of sFlt-1 measurement. This biochemical marker appears to be a promissory predictor of preeclampsia.

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Spatio-temporal expression patterns of progranulin in the human placenta and control of its regulation by steroid hormones

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Progranulin (PGRN, syn. acrogranin, PCDGF, granulin-epithelin precursor) is a pleiotropic glycoprotein that stimulates cell migration and proliferation, shows anti-inflammatory activities in wound healing processes and is involved in developmental events like male-specific brain differentiation. The expression of PGRN is partially regulated by steroid hormones (e.g. in MCF-7 breast cancer cells). In-vitro studies on mice revealed a strong expression of PGRN in trophectodermal cells and demonstrated stimulating effects on blastocyst hatching and cavitation as well as outgrowth and proliferation of trophoblast cells. Assuming a functional relevance of progranulin also in human implantation processes we studied the protein expression patterns in first and third trimester human placenta specimens. Strongest expression was seen in the trophoblast cells of the first trimester. Levels clearly decreased in term placenta tissue. Moreover amniotic fluid of second trimester contains high levels of PGRN. We further used primary cultures of human trophoblast cells for investigating the influence of steroid hormones on PGRN expression. Therefore we analyzed the cellular mRNA expression as well as the protein levels of supernatants. All tested hormones (17-β estradiol, progesterone, prednisolone, dexamethasone) did not show any influence on progranulin synthesis.

In conclusion we demonstrated for the first time a strong PGRN expression also in human trophoblast cells of the first trimester. Further, progranulin is secreted by cultured throphoblast cells, but it remains actually unclear how its expression is regulated. Our Results strongly suggest an impact of progranulin also in human placentation, but further studies regarding the investigation of functional mechanisms are needed.

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Phenylephrine (PE) sensitivity is not affected by cyclooxygenase (COX) and nitric oxide (NO) pathways in mesenteric veins of pregnant rats

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Increased venous return is thought to be important in the cardiovascular adaptation to pregnancy. The purpose of this study was to test whether the blunted alpha1-adrenergic sensitivity in mesenteric veins of pregnant rats can be explained by interaction with COX pathway and/or NO synthase? Mesenteric veins from cycling (NP, n=27) and age matched late pregnant (LP, n=24, day 19-21) Sprague-Dawley rats were dissected and cannulated in a specialized venograph system. By using pressurized (6mmHg) venous segments from anatomically similar locations, lumen diameter was measured continously with a video-electronic system. Venous endothelium was removed mechanically by using first a human and then a horse hair. Complete endothelial removal was confirmed by electron microscopy. The veins from LP rats were less sensitive to PE than NP controls (EC50: 109nM vs. 31.4 nM, p<0.05). Meclofenamate (MF), which blocks conversion of arachidonic acid, and N-nitro--L- arginine methyl ester (L-NAME), which inhibits endothelium-dependent NO synthase, had both no effect on the PE-venoconstrictor response of the LP and NP groups (EC50: 119nM vs. 42.6nM and 83.5nM vs. 46.2nM, n. s.). Compared to the effects of L-NAME, venous PE-sensitivity was mimicked by endothelial removal (EC50: 105nM v. s. 51.2nM, n. s.). These data indicate that under these conditions: (1) Pregnancy decreases the vеноoconstrictor response to PE.(2) This decreased venous alpha1-adrenergic sensitivity is not mediated by products of COX pathway and NO synthase.(3) The effects of L-NAME and endothelial removal are the same.

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Usage of antithyroid peroxidase antibody (anti-TPO Ab) for assessment of subclinical hypothyroidism in first trimester of pregnancy


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Background: Hypothyroidism during pregnancy has been found in 2.5% of all normal pregnancies and untreated hypothyroidism may lead to miscarriage and preterm delivery. In clinical practice hypothyroidism is characterized by a high level of thyroid stimulating hormone (TSH) even with no overt thyroid dysfunction. The aim of this study was to evaluate pregnant women with subclinical hypothyroidism in first trimester.

Methods: Serum Fasting Blood Sugar (FBS), Total Thyroxin (T4), Anti- TPO antibody and Complete Blood Cells (CBC) were determined in 92 pregnant women who recruited from the Razi Pathobiology Laboratory, Karaj, Iran during 2008. The including criteria was age before 40 years, no history of previous thyroid disease and diabetes mellitus in first trimester of pregnancy. Hypothyroidism was defined as TSH more than 5.1mIU/L and positive anti-TPO antibody was more than 20IU/ L.

Results: Average age was 27.7±4.2 years; gestation age was 14.7±1.5 weeks; an elevated TSH with normal T4 was found in 4.5% on the pregnant women. Anti-TPO antibody was positive in 16.4% on the pregnant women.

Conclusion: Our data suggest that anti-TPO antibody may be better marker than TSH to identify pregnant women with subclinical hypothyroidism during first trimester and more studies are needed.

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Thyroid function study of women during pregnancy

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Aim: To study and document the changes in the function of the thyroid gland during pregnancy, given the fact that due to estrogen production the thyroxine binding globulin of the liver increases. As a result, the amount of bound hormones increases and the amount of free thyroxine decreases, leading to hypersecretion of TSH and thyroid gland hyperplasia.

Material – Method: Material for our study were 685 pregnant women, in whom we determined immunoenzymically, using the chemiluminescence method, the T3, T4, FT3, FT4 and TSH hormones.

Results: a) In 547 women (79.85%) no disorder was found, b) In 127 women (18.54%) high values of T3 and T4 were recorded with normal levels of FT3, FT4 and TSH. In a follow-up test (six months after labor) T3 and T4 values were restored fully to normal levels. c) In 11 women (1.61%) high values of T3, T4, FT3, FT4 were recorded, with low TSH value. Their hyperthyroidism was confirmed and treated with medication, by administering the minimum possible dose, while the thyroid function tests of the neonates after parturition came out normal.

Conclusions: Therefore, it is proven that hyperthyroidism is not unlikely during pregnancy, either hyperthyroidism can manifest during pregnancy, or a woman already suffering from hyperthyroidism can become pregnant. Certainly, special attention is needed in the diagnosis of these cases, considering the fact that hyperthyroidism symptoms such as tachycardia, thermophobia etc. are attributed to pregnancy, while a possible weight loss is covered by the weight gained during pregnancy.

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**Reactive oxygen substances (ROS) and total antioxidant defences (TAD) on cord-blood of full-term healthy babies**

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Introduction: ROS are implicated in many severe neonatal diseases as bronchopulmonary dysplasia, necrotizing enterocolitis, intraventricular haemorrhage, periventricular leukomalacia, retinopathy of prematurity. TAD are the natural defenses the organism has to counteract ROS.

Patients and Method: We have measured both ROS and TAD at birth on cord-blood of consecutive full-term healthy babies with a bed-side equipment (Callegari 1930, Parma, Italy).

Results: Eighty-one babies were enrolled, 41/81 were males, 34/81 vaginal deliveries and 47/81 elective CS. Mean value of ROS was 131.1±76.1 and mean value of TAD was 1.39±0.74 mmol Trolox equivalent. A direct relationship was found between ROS and PaO2. An inverse relationship was recorded for TAD and ROS.

Discussion: The mean value of ROS found is lower than that of adults. This can be explained by the lower PaO2 the fetus is exposed in utero. The mean value of TAD is in the range of the adult value, meaning probably that the baby is ready to face the higher concentration of oxygen of room-air.

Conclusion: ROS and TAD are strictly related each other. Any prenatal disease (e.g. chorioamnionitis) could increase the value of ROS. Peculiar situations (e.g. prematurity, chronic fetal distress) can reduce the value of TAD. When both situations are present at the same time they can facilitate the development of the aforementioned disease. More studies on preterm infants and on specific diseases are necessary to confirm these hypotheses and find possible preventive strategies.

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Documentation of platelet number changes during pregnancy


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Aim: Study of documented changes in platelet concentration during pregnancy as well as during labor. It concerns a comparative study between cases of normal pregnancy and pathological situations.

Material – Method: The study involves 158 pregnant women, out of which 118 had a normal pregnancy, 16 presented toxinaemia, 13 diabetes mellitus and 11 several other pathological situations. Simultaneously, platelet concentration of a group of 100 healthy women of similar (reproductive) age was studied with the pregnant women in our study. These 100 women constituted the control-martyr group.

Results: It was proven that women with normal pregnancy do not present a statistically important disorder of platelet concentration in regard to the control group (increase of average value of platelets number <5%). Nevertheless, women with pathological pregnancy presented a substantial increase in platelet concentration. The documented increase of the average value of platelet concentration was approximately 65% in pregnant women with hypertension and it was even greater, approximately 110% (doubling of platelet concentration) in pregnant women with diabetes mellitus.

Conclusion: 1) It is proven that platelet behavior ranges during pregnancy to an extent that it varies proportionately and it depends on the kind of the coexistent illness, presenting a substantial increase in the case of hypertension and mainly in the cases of pregnant women with diabetes. 2) Therefore, it is of great significance for the attendant doctors to take this in to consideration, given the fact that the number of platelets is very important for hemostasis during pregnancy.

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Study of the changes of coagulation factors during pregnancy

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Aim: To investigate the changes of the factors related to the coagulation mechanism during pregnancy and to estimate the magnitude of hypercoagulation that they cause.

Material - Method: In our study 72 parturients were included who, among other lab tests, were tested from the 2nd trimester of pregnancy onwards with complete blood count as well as tests related to blood coagulation including prothrombin time (PT), partial thromboplastin time (PTT) and also fibrinogen (FIB).

Results: PT<12 sec was found in 34 women (47.2%), PTT>40 sec in 11 women (15.3%), while FIB>4g/l was found in 63 women (87.5%) of whom 11 (15.3%) had FIB>6g/l. Lastly, in regard to platelets, in 12 cases (16.7%) a platelets number lower than 140,000 was found – this was certified by microscopy examination of peripheral blood films – and in almost all cases, a decrease was recorded in following check-ups as pregnancy progressed.

Conclusions: Consequently, it is proven that in many cases (42.7%) PT decreases during pregnancy, while in fewer cases (15.3%) an increase of PTT is recorded. Also, in the vast majority of cases (87.5%), fibrinogen is increased – and in some of them significantly increased –, while often there is a low platelets number, that continues to decrease as pregnancy progresses. Therefore, there is a great need of conducting the tests necessary to evaluate the coagulation mechanism in every pregnant woman – the earlier the better – and particularly in high risk women.

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Spontaneous apoptosis of monocytes in cord blood of healthy full-term newborns

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Background/Aims: CD95 molecule (Fas) and its ligand (FasL) CD95L are expressed and are functional in mediating cell death in cord blood mononuclear cells. They play important role in the homeostasis of haematopoetic cell populations. CD95 is receptor mediating a signal for cell death by apoptosis. Its inducible ligand has been demonstrated to mediate cell death of multiple types of CD95 expressing cells. We have examined whether the gender affect the expression of these parameters.

Patients and Methods: We included in our study 24 full term newborns: 13 females (F) and 11 males (M). Blood was obtained from the umbilical artery and Fas, FasL and Bcl-2 were determined by flow cytometry.

Results: In term newborns we have found 82.93% of Fas, 14.34% of FasL and 21.39% of Bcl-2 monocytes expression. We have found higher expression of Fas on female monocytes 85.60% in comparison to male monocytes 80.27%. FasL was less represented on female monocytes 13.50%, than in male monocytes 15.18%. The Bcl-2 is a lower demonstrated on female monocytes 20.68%, in contrast to male monocytes 22.11%.

Conclusion: We did not find distinct difference in expression of Fas and FasL on cord monocytes in relation to gender. It concern also expression Bcl-2.

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SciCoMed – a new scientific research database-platform makes science manageable

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E-Science describes a new form of the web-based scientific work. It is aim of SciCoMed to create a neutral platform for scientific research in order to enable better communication within a research team and to facilitate data sharing with the rest of the scientific community. SciCoMed helps to identify and maximize opportunities for international cooperation. Uniform documentation sheets guarantee high data quality. Every research group manages their data autonomously by using a user name and password. Own data sets are visible only for registered Data-Manager. Only after arrangement the data are provided for cooperation projects. So every Data-Manager is integrated into the network without losing his individuality. SciCoMed will contribute to the ambitious goal of “maximum possible benefit” by reducing costs and time required for a study. This is especially an important aspect for many companies. Being part of this network it is easier to find suitable sponsors. For this reason a profile-searching module has been created on the platform. This serves to find and/or to be found more easily. Every researcher has the possibility of announcing his research interest and expertise. Also companies have the possibility of describing their profile.

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The role of recombinant human erythropoietin in the treatment of iron deficiency anemia of pregnancy

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Introduction: The purpose of this study is the evaluation and management of iron deficiency anemia in pregnancy using recombinant human erythropoietin combined with oral iron in severely anemic pregnant. It is followed the practice of some centers which have chosen to use slightly lower Hb values (<11gr/dl) to define anemia during pregnancy remembering to obtain a follow up hem gram.

Method-Material: Forty (40) pregnant were diagnosed as suffering from severe iron deficiency anemia at the Maternity Clinic of Pyrgos, the last five years. These women were treated with recombinant human erythropoietin (10000 IU given SC every other day that means three times weekly) in combination with oral iron. The dose was 1600mg of proteinsuccinylate iron daily. The therapy lasted four weeks and was initiated at the end of second Trimester or alternatively in the third Trimester. The inclusion criteria are described below: Hem globulin (Hb) below 8.5gr/dl, hematocrit (Hct) <26%, low serum ferritin levels (<10µg/dl), red used total iron –binding capacity (<216µg/dl) and abnormal erythroid RBC indices (MCV, MCH, MCHC). A second group of twenty (20) severely anemic pregnant were treated with blood transfusion. The mean value of transfused units was four (4) per woman per month. All women were matched for age and parity and signed informed consent. The Results were collected and evaluated according the mean elevation of Hb and Hct values. The two groups were compared using the Student’s t-test.

Results: The majority of iron deficient anemic pregnant reacted promptly in the combined erythropoietin and supplemental oral iron treatment in the first two weeks of therapy. The mean elevation of Hb value was 2.7gr/dl and Hct value was 8.1%. Two pregnant did not respond to treatment and needed the transfusion of two blood units each. The groups of pregnant who treated with blood transfusion raised Hb at a mean value of 2.9gr/dl and Hct 8.7% respectively. Additionally one pregnant presented anaphylactic reaction in the transfusion group and was treated with prednisolone IV. The statistical analysis of the Results of the two groups did not disclose any statistically significant differences in the elevation of Hb and Hct. For the statistical assessment the Student’s t-test was used.

Conclusion: The use of erythropoietin in severe iron deficiency anemia during pregnancy is not considered to be a standard treatment. In our study proved to be very effective with limited adverse effects. The effective combination of recombinant human erythropoietin SC and elemental iron orally in the severely iron deficient anemic pregnant may also assist in the dramatic reduction of the need in blood transfusion during pregnancy.

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Sildenafil citrate as a therapeutic agent in neonates with persistent pulmonary hypertension

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Background: Persistent pulmonary hypertension of the newborn (PPHN) presents high mortality rates despite the use of high frequency oscillatory ventilation (HFOV) and inhaled nitric oxide (iNO). Advanced therapeutic approaches include oral sildenafil that may cause selective pulmonary vasodilatation, therefore improving gas exchange in PPHN patients.

Objective: To evaluate the effect of sildenafil citrate on oxygenation in confirmed PPHN.

Patients and methods: We studied five term neonates who were admitted to the NICU with severe respiratory failure in the first 24 hours of life from July to March 2008. In all cases, PPHN was confirmed with echocardiogram and was managed with HFOV combined with iNO. Sildenafil solution of 1mg/kg per dose was prepared from a 50mg-tablet and administered by orogastric tube at 3 hour intervals. Arterial blood gases and oxygenation index (OI) were evaluated at 1 hour after each dose. Blood samples were obtained via an umbilical artery catheter.

Results: All infants presented a statistically significant improvement of OI after the administration of first dose sildenafil solution (mean OI before administration: 20.8, ranging from 11 to 33.4 while after administration: 6.8 with a range of 2.07-16, p=0.047). Two infants died, one due to air leak syndrome and one due to severe respiratory failure unresponsive to treatment. OI was higher in these cases.

Conclusions: Sildenafil proved to be more efficacious when introduced before the establishment of severe PPHN. Addition of oral sildenafil appears to be useful in the management of PPHN in a well-equipped NICU.

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Measurement of female tumor markers ca-125 and ca -153 during pregnancy

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Aim: To determine the values of tumor markers CA-125 and CA-153 in pregnant women the first trimester of their pregnancy. As we know: a) the tumor marker CA-125 increases in serous ovarian cystadenocarcinoma, in cancer of the pancreas, breast and lung, also in benign diseases like endomitriosis and in pregnancy (especially in the first trimester) and b) the cancer marker CA-153 increases mainly in cases of women with breast cancer (primary or metastatic).

Material-Method: Material for our study were 307 women in their first trimester of pregnancy who were tested for CA-125 and CA-153 tumor markers at the immunological laboratory, using an immunoenzymic analysis method.

Results: a) In 251 pregnant women (81.7%) the tumor markers were at normal levels, b) in 39 (12.7%) tumor marker CA-153 was normal whereas CA-125 was elevated, c) in 12 (3.9%) CA-125 was normal whereas CA-153 was elevated, and d) in 5 (1.6%) both markers were elevated. After a three month period from the end of their pregnancy, follow-up tests were performed who showed normal values for the tumor markers, while no malignancy appeared in any of the women.

Conclusion: It is proven that the tumor marker whose values rise during pregnancy at a greater percentage (12.7%) is CA-125, while, after the end of the pregnancy almost every time the marker values return to normal levels.

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Aflatoxin absorption from the gut of pregnant mice and its appearance in the fetus

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Background: Aflatoxins exposure occurs through largely contaminated food and diary milk. We studied the pharmacokinetics of aflatoxin in mice and characterized IUGR. Methods: Aflatoxin B1, freshly mixed at various times with DMSO, was administered intraperitoneally to groups of mice in single doses of 40mg/kg on GD13 and orally through an orogastric tube. The controls received a proportionate volume of DMSO only. The fetuses were collected on GD18, weighed and observed for visceral and cartilage and bone anomalies and growth delay. Maternal blood, and fetal blood were collected at 15, 30, 45, 60, 90, 120 and 150 minutes post-treatment in other groups of mice. AFB concentrations following maternal exposure to AFB were correlated with liver and placental pathology and fetal effects.

Results: The serum concentrations were predictable and the highest serum levels were seen immediately at 15 minutes in mice given aflatoxins intraperitoneally and slightly later in those given it orally. The mice receiving aflatoxin produced embryos with lower weights than those which did not receive aflatoxins.

Conclusion: Aflatoxins are quickly absorbed whether given orally or intraperitoneally and reach peak levels within 30 minutes. Given in the 3rd trimester it produces intrauterine growth retardation.

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Estradiol inhibits hif-1α expression in first trimester villous explant cultures

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Objective: Expression of Hypoxia inducible factor-1 (HIF-1α) in placenta is high in early gestation between 5 to 8 weeks and then falls precipitously around 10 to 12 weeks of gestation. HIF-1α inhibits trophoblast differentiation toward an invasive extravillous trophoblasts (EVTs). Estradiol begins to rise in 6-8 weeks of gestation when placental function becomes apparent. It has been reported that estradiol inhibits hypoxia induction of HIF-1α in Hep3B Cells. In this study, we investigated the effects of estradiol on expression of HIF-1α and trophoblast differentiation in human first trimester villous explant cultures.

Study Design: Villous explant cultures were established from first trimester human placentas (6-8 weeks of gestation, n=3) obtained from elective terminations of pregnancies. Normal villous tissues were explanted on matrigel and incubated under 3% O2 tension for 5 days. In the experiments evaluating the effect of estradiol, 1ng/mL of estradiol was added to the culture medium. Morphological integrity and viability of villous explants were monitored. Expression of HIF-1α in villous explant cultures was evaluated by Western blotting.

Results: EVTsoformed outgrowth of cells from the distal end and invaded the surrounding matrigel. As compared with control villous explants, exposure of villous explants to estradiol showed a decreased outgrowth of cells from the distal end. However, estradiol treatment increased invasion into the surrounding matrigel. On western blots, the expression of HIF-1α decreased after treatment with estradiol under 3% O2 oxygen tension.

Conclusion: These findings suggest a possible role for estradiol to mediate trophoblast differentiation toward an invasive EVTs by interfering with increases in HIF-1α levels.

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The effects of electromagnetic field (EMF) on development of ovary in rat
(A light microscopic study)

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Background, Objectives: With the increase in modern technology, many industrial and household appliances, which we take for granted to be safe expose the public to magnetic fields. Various studies using rodents as experimental models have attempted to elucidate the reproductive toxic effects of exposure to weak magnetic fields and the results have been found to be rather contradictory. During the last decade, geniculare systems have been extensively studied and their vital importance for normal function is generally accepted and established their role in their regulation for spermatogenesis and oogenesis. The aim of this study was to evaluate the effects of Electromagnetic field (EMF) on in-vitro rat postnatal ovary development.

Methods: A total of 40 male and 40 female Wistar rats (about 15 week-old) procured from animal house were used for the study. The equipment was based on Helmholtez coil which works following Fleming's right hand rule. The experimental pups were exposed to EMF till five weeks of postnatal age.

Results: It showed heterochromatism and condensation of oocyte cell nucleus. Depopulation of follicles were seen. The empty spaces between the granulose and theca cells appeared.

Interpretation, Conclusion: The results suggest that EMF exposure causes profound changes in the ovary on long term exposure it could result in irreversible damage which may lead to sub fertility. It is suggested that long term exposure should be avoided.

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Pluripotent stem cells isolated from human amniotic fluid and differentiation into pancreatic β-cells

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Human amniotic fluid (HAF) contains multipotent stem cells (AFSCs) which can differentiate into a variety of different cell types. Recently, we demonstrated that obestatin, a peptide encoded by the ghrelin gene, exerts antiapoptotic effects in pancreatic β-cells and human islets and increases the expression of genes involved in β-cell differentiation. We investigated whether: 1) AFSCs would differentiate into pancreatic β-cells and 2) obestatin would increase β-cell differentiation from AFSCs.

Amniotic fluid was collected from women undergoing prenatal amniocentesis with informed written consent. Samples of the AF were cultured in selection media (Knockout DMEM + Knockout Serum Replacement + glutamax + penicillin/streptomycin + nonessential amino acids + 2-mercaptoethanol + recombinant human bFGF + Activin A). FACS analysis and immunocytochemical staining showed the presence of mesenchymal and endothelial markers in AFSCs. Real-time PCR evidenced the expression of Oct-4, a marker of pluripotency, during early differentiation phase. However, the β-cell differentiation marker duodenal homebox factor-1 (PDX-1) could not be detected. Obestatin increased Oct-4 expression but had no effect on β-cell differentiation. These Results suggest that, at least under the experimental conditions used in this study, AFSCs do not differentiate into β-cells and obestatin has no effect on β-cell differentiation.

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Novel in vitro model for evaluating the molecular link between oxidative stress and neural tube defects

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Introduction: Oxidative stress, involved in the aetiology of defective embryonal development, can alter most types of cellular molecules, inducing metabolic dysfunction and developmental block. Hyperglycaemia-induced oxidative stress during early diabetic pregnancy increases the risk for neural tube defects. Although oxidative stress has been shown to repress embryonal transcription of Pax-3, a primary lineage control gene required for neural tube closure, the molecular mechanism underlying oxidative stress-induced Pax-3 repression is unknown. The molecular link between sublethal oxidative stress and defective embryonal development remains unclear.

Methods: P19 embryonal carcinoma cells, able to differentiate into all three germ layers, provide an in vitro assay for neural induction and differentiation. P19 cells were exposed to tert-butylhydroperoxide (tbHP) (0,5,20µM) for 36h while differentiating in suspension in bacterial grade tissue culture plates (n=3). Cell viability was then evaluated using light microscopy. Each test was performed 3 times.

Results: 5µM tbHP was sublethal for all P19 cell cultures in all 3 tests. In contrast, 20µM tbHP killed all P19 cell cultures in all 3 tests.

Discussion: Although oxidative stress has been shown to induce Pax-3 repression, the molecular link between sublethal oxidative stress and neural tube defects remains unclear. Here we establish a novel in vitro model to evaluate the molecular link between sublethal oxidative stress and neural tube defects. We hypothesize that sublethal oxidative stress decreases cellular methylation potential, causing epigenetic inhibition of Pax-3 transcription. Future research using this model may reveal the molecular link between sublethal oxidative stress and congenital birth defects.

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Study of the prevalence of cardiovascular risk factors in women with medical history of gestational diabetes


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Aim: To estimate the prevalence of cardiovascular risk factors in women with medical history of gestational diabetes.

Material-Method: 32 cases (group A) of women with the average age of 39.4 years, who presented gestational diabetes without any case of later appearance of type II diabetes, were included in the study. The lipidemic profile was examined, the existence of metabolic syndrome according to NCEP criteria was investigated, while the Results were compared to those of 40 other women (group B), of similar age and BMI, without gestational diabetes.

Results: The prevalence of the metabolic syndrome was almost the same. Nevertheless, 17 women in group A (53.1%) presented 2 out of the 5 criteria, comparing to only 6 women (15%) of the control group. Although the average levels of HDL cholesterol did not differ, 12 women in group A (37.5%) were found with HDL-C level <45mg/dl, comparing to 7 women (17.5%) in group B. Moreover, in group A the average level of triglycerides was much higher, and 15 out of the 32 women (46.9%) presented levels >150mg/dl, comparing to 3 women (7.5%) in group B. Finally, coexistence of triglycerides level >150mg/dl and HDL-C level <45mg/dl was found in 11 women (34.4%) in group A, while none of the women of the control group presented similar values.

Conclusions: It is, therefore, proved that the cardiovascular risk factors and particularly the lipidemic ones, appear more often in women with medical history of gestational diabetes in relation to other women.

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**Myocardial response in preterm fetal sheep exposed to a fetal inflammatory response syndrome**

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Chorioamnionitis (CA) is associated with increased proinflammatory cytokines in amniotic fluid. Intravenously administered endotoxin to chronically instrumented fetal sheep is well known to induce fetal inflammatory response syndrome (FIRS) which increases perinatal morbidity and mortality. We studied whether the fetal myocardium is affected by the FIRS. To this purpose, mRNA levels of toll-like receptor 2 and 4 (TLR2 and TLR4), hypoxia-inducible factor 1α (HIF-1α) and inducible NO-synthase (iNOS) in fetal ovine myocardium were determined.

Twelve fetal sheep were chronically catheterized at a mean gestational age of 110±1 days (0.7 of gestation) and exposed to the bacterial endotoxin lipopolysaccharide (LPS =100ng, E.coli, 0127:B8) n=6 or saline n=6. Fetuses were delivered via c-section three days after surgery. Gene expression was measured by real-time PCR with ovine-specific primers. We found a 4.4-fold increase for TLR2 mRNA, 5.7-fold for TLR4 mRNA, 5.8-fold for HIF-1α mRNA and 3.0-fold for iNOS mRNA in the FIRS group compared to the control group.

Our results indicate that FIRS induced myocardial hypoxia and that there were changes in mRNA level of pattern recognition receptors. Similar changes in adults have been associated with cardiac dysfunction. Further research is needed to compare fetal myocardial changes in FIRS to adult.

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Intraamniotic endotoxin induced chorioamnionitis alters fetal thymus function


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Background: The fetal thymus is essential for the development of T-lymphocytes. Regulatory T-lymphocytes mediate homeostasis of the immune system and differentiate under the control of the transcription factor FoxP3 in the thymus. The effects of fetal inflammation caused by chorioamnionitis on thymus development and function are not well understood.

Methods: Chorioamnionitis was induced by a single intraamniotic injection of LPS 5h, 1d, 2d or 5d before delivery of preterm lambs at 123d gestation age. Cord blood lymphocytes, plasma cortisol and thymus weight were quantified. Corticosteroid receptors-, NF-κB- and FoxP3- positive cells were evaluated by immunohistochemistry.

Results: Lymphocytes were decreased by 40% after 1d in the endotoxin group. Thymus weight was reduced, with a 40% decrease at 5d. Endotoxin increased the plasma cortisol concentration with a maximum of 2.6-fold after 2d without affecting the expression of the corticosteroid receptor in thymus. In addition, endotoxin increased NF-κB signalling and reduced the number of FoxP3 positive cells to a minimum at 1d of 60%. These observed changes were no longer evident after 5d.

Conclusion: This antenatal inflammatory sequence underlines chorioamnionitis induces changes in fetal thymus which may have implication on the development of immune functions in preterm infants in later life.

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Development of a standardized method to sterilize and preserve amniotic membrane grafts

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Objective: Amnion grafts have been used in experimental models and clinical practice to encourage epithelialisation as a wound dressing for severe burns, skin ulcers and for the treatment of ophthalmologic diseases. There still does not exist any standardized method to sterilize and preserve amniotic membranes (AM). We examined biophysical and histological characteristics of AM which were sterilized and preserved by different techniques in order to find a method that complies with International Standards (Council of Europe, EATB Standards).

Methods: AM were prepared by 3 different methods: sterilization with peracetic acid and glycerol conservation [GLY] respectively AIR-drying [AIR] and preservation at -80°C without sterilization [-80°]. Tear strength and sulphur content were measured and fibrillar collagen Type V and VII (Sigma C6805) were determined as components of the basement membrane.

Results: The tear strengths were 18 N/cm² [AIR], 10 N/cm² [GLY] and 5 N/cm² [-80°]. The mean concentrations of sulphur were 34.5 Edx-Units [AIR], 24.9 units [-80°] and 13.9 units [GLY]. The typical structure of the AM was preserved by all methods. Collagen Type VII was clearly detectable in [-80°], scarcely in [GLY] and not traceable in [AIR]. Collagen type V was scarcely detectable in [GLY] and [-80°].

Conclusions: The Results confirm the findings of the pilot survey of von Versen et al. (2004). The AM which were sterilized with peracetic acid and preserved by air-drying showed higher tear strength and sulphur concentration suggesting better biophysical properties compared to the two other methods (p<0.05). In addition the use of a validated sterilization procedure guarantees safety of infections.

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Cells cultured from amniotic fluid cells contribute to recovery from acute renal injury

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We injected cells cultured from human amniotic fluid (AF) in SCID mice with experimental acute renal injury to evaluate whether they aid in the process of renal regeneration.

Amniotic fluid was collected from women undergoing prenatal amniocentesis with informed written consent and approval of the ethic committee. Samples of the AF were cultured in selection media (Alpha MEM + Amniomax + FCS + Glutamine + Pen/Strep + Primocin).

Cytofluorimetric analysis showed that AF cells are positive for CD44, CD73, and CD166 and partially for Oct4 and SSEA4. Later passages are also positive for CD105. CD45 is negative.

We successfully differentiated AF cells into osteogenic, demonstrated by the accumulation of calcium (Von Kossa), adipogenic, demonstrated by lipid vesicles formation and their Oil Red O coloration, and chondrogenic cells, demonstrated by the presence of hyaluronic acid and sialomicin (Alcian Blue) in the cellular aggregate treated with paraffin.

Experimental injury was induced in SCID mice by glycerol injection. At day 3, animals received AF cells by tail vein injection. Control animals received injection by saline.

We found a significant increase of proliferation counting BrdU- and Pcna positive cells/per optical field in tissue biopsies from day 5: in the AF cells injected mice BrdU was 10.1 ± 6.8; Pcna: 10.8 ± 7.3, in control animals BrdU 0.85 ± 1.1; Pcna: 3.55 ± 2.8.

BUN measured: in untreated control animals was 107 ± 7mg/dL, while in AF treated animals were reduced to 47.8 ± 24.5mg/dL. Our Results suggest that AF cells contribute to regeneration by promoting repair of tubular structures.

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High salt intake in pregnancy alters maturation of rat glomeruli

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Faulty fetal programming leads to alterations in offspring’s kidney morphology. Low number of glomeruli is known to cause high blood pressure later in life. It has been suggested that high salt intake during pregnancy influences blood pressure in the offspring. It was the purpose of the present study to clarify whether high salt intake in pregnancy alters kidney development in the offspring. Sprague-Dawley rats were fed normal (0.15%), medium (1.3%), or high (8.0%) salt diet during pregnancy and weaning. Kidney morphology was assessed at 1 week postnatal and expression of proteins of interest at term and at 1 week of age. At age 1 week the number of S-shaped bodies was significantly lower (405±308) and the number mature glomeruli (818±405) and layers of developing glomeruli (7.1±0.6) was higher in the offspring of mothers on high-salt compared to the other groups (1044±490, 460±304, and 5.9±0.9 respectively). As a net Result total number of glomeruli was significantly lower in the offspring of mothers on high-salt (9476±1264) compared to the other groups (11175±1920). At 1 week of age in the offspring of mothers on high salt the glomeruli were bigger compared to lower salt intake. The expression of Pax-2 and FGF-2 was significantly lower in the offspring of mothers on high-salt consistent with their causative role. However there was no difference between the groups in litter size, birth weight, and placenta size. We conclude that high salt intake during pregnancy accelerates maturation of glomeruli in the offspring, but reduces their final number.

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Basal Body Temperature and Endometriosis

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Abstract: This investigation examined the association between pelvic endometriosis and altered Basal Body Temperature (BBT). This study population consisted of infertile couples who have been diagnosed as having endometriosis. A significant association was found between the presence of pelvic endometriosis and the appearance of a late decline in BBT during the early follicular phase of the menstrual cycle. A temperature of 97.80°F on the first 3 days of the menses is associated with pelvic endometriosis. The findings of this study support the clinical diagnosis of endometriosis in infertile women. The basal body temperature chart analysis may be useful as a clinical adjunct when endometriosis is suspected.

Key world: BBT (Basal Body Temperature): P (Pregnenolone): PF (Paritoneal fluid) PG (Prostaglandin)

A relatively common problem in women is endometriosis. The association between endometriosis and infertility is clearly established. It is proposed that endometriosis has the potential to produce pathology in two ways
2. Peritoneal inflammatory response.

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Higher circulating antiangiogenic endostatin, but not angiopoietin-2, decreases pregnancy potential in IVF cycles

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Objective: To analyze the potential role of angiopoietin-2 and endostatin in infertility.

Background: Infertility is a growing problem and 10-20% remains unexplained. Disturbances in angiogenesis could contribute to unexplained infertility. In animal studies, disturbances in expression of proangiogenic VEGF-A and its soluble receptor sVEGFR-1 impair reproductive angiogenesis and decreases fertility. Information about angiopoietin-2 and endostatin, antiangiogenic growth factors that together with proangiogenic growth factors such as VEGF-A act to shape and direct angiogenesis, and infertility in humans is limited.

Methods: In a case-control study, women with unexplained infertility (n=20) and tubal infertility (n=18) were recruited. Blood samples during normal menstrual cycle and in vitro fertilization (IVF) cycle were analyzed with ELISA. Patients were compared with respect to both infertility and pregnancy outcome.

Results: Angiopoietin-2 did not vary significantly during the IVF cycle or between pregnancy outcome groups. No differences in angiopoietin-2 or endostatin concentrations between infertility groups were found. Endostatin concentrations (ng/mL, median (range)) were significantly higher during the IVF cycle (79.6 (42.5-143.2) than during the normal cycle (66.2 (39.7-90.1), p<0.0001). Higher endostatin both in the normal cycle (69.4 (44.7-85.2) vs. 56.1 (40.0-80.4), p=0.015) and the IVF cycle (88.2 (56.7-143.2) vs. 78.4 (52.6-95.3), p=0.006) associated with negative pregnancy outcome.

Conclusions: The significant variability of endostatin both between the normal menstrual cycle and the IVF cycle and within the IVF cycle indicates that endostatin participates in reproductive angiogenesis. Importantly, higher endostatin predicted negative pregnancy outcome. A higher endostatin concentration could disturb the reproductive angiogenic balance, contributing to decreased fertility.

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Anatomopathological findings in placentas of patients with suspicion of fetal intrapartum hypoxia

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Objective: to learn about the most frequent placental pathologies in patients with diagnose of fetal intrapartum hypoxia.
Method: 316 cases of patients with suspicion of fetal intrapartum hypoxia at this hospital were analyzed from May 2006, through March. We conducted an anatomopathological study of the corresponding placentas.
Results: 72% of placentas were studied, 40% of them evidenced maternal vascular pathology (15% low flow, 9% placental infarction, 7% acute ischemia, 3.1% maternal floor infarction), 15.8% showed postmature placentas, 7% fetal vessel obstruction, 6.2% were infection-caused pathologies (3.2% cytomegalovirus, 3% chorioamnionitis), and last, 3% of placentas were normal.
Conclusions: The most frequent findings for placental pathologies in patients with suspicion of fetal intrapartum hypoxia were maternal vascular pathology and placental postmaturity.

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Is there any correlation between birth weights of future mothers and their risk to develop hypertensive diseases in pregnancy?

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Background: Despite an intensive research the aetiology of hypertensive diseases in pregnancy remains unclear. According to the model of fetal programming it seems likely that the birth weight of a future mother is associated with an increased risk to develop hypertensive diseases in pregnancy (HDP). We therefore investigated this correlation in women with HDP compared to controls.

Methods: A self-administered questionnaire developed for the current study was completed by 142 women with HDP and 124 matched (age, nationality, education, parity) control women. The index-pregnancy in cases was defined as the first pregnancy conducted beyond the 24th gestational week which was complicated by HDP. Women had to report their own birth weight as well as their waist and the hip circumference in order to be able to calculate their waist-hip ratio at the beginning of the index-pregnancy.

Results: Mean own birth weight in women with HDP was 2932.5g compared to 2947.7g in controls which was not statistically significant. Also there was no difference in waist hip ratio.

Conclusion: Own birth weight does not seem to play a role in the risk for HDP.

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Is snoring a risk factor for hypertensive diseases in pregnancy?

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Background: Hypertensive diseases in pregnancy (HDP) are still one of the leading causes of maternal and fetal perinatal deaths. Recent research results support the hypothesis that snoring may be associated with an increased risk to develop HDP. On this background the current study investigated whether snoring is a risk factor for HDP.

Methods: A questionnaire developed for the current study was completed by 142 women with HDP and 124 matched (age, nationality, education, parity) control women. The index-pregnancy in cases was defined as the first pregnancy conducted beyond the 24th gestational week which was complicated by HDP. All diagnoses were verified by medical charts and differentiated according to the criteria of the ISSHP. Women were asked whether they or their partner had remarked snoring and/or sleep apnoe during pregnancy.

Results: Of the women with HDP 11.3% and of the controls 4.8% reported snoring during pregnancy which was not statistically significant (p=0.0955). According to the estimation of themselves and/or their partners one of the cases and none of the control women suffered from sleep apnoe.

Conclusion: The presented results do not confirm former results reporting an increased risk for HDP in women snoring during their pregnancy.

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Is professional activity a risk factor for hypertensive diseases in pregnancy?

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Background: Hypertensive diseases in pregnancy (HDP) remain one of the main causes for perinatal maternal and fetal deaths. Different research Results support the hypothesis that professional activity is a risk factor for HDP. The current study investigated whether professional activity is associated with an increased risk for HDP. Methods: A questionnaire developed for the current study was given to 2600 women, who had contacted the German pre-eclampsia self help group (Gestosefrauen e.V.) for information on HDP and to 1484 controls. Women were asked about part- and full time professional activity during pregnancy. They had to report the type of work, the amount of part- or full time work as well as their working time related to gestational age. After confirmation of diagnoses according to medical charts and after matching for age, nationality, education and parity, data from 707 women with HDP and 560 controls could be evaluated.

Results: Women with HDP do not differ in professional activity from controls. 77.7 of the cases and 76.4% of the controls worked full time. The percentage of women with part time activity was 13.6% and 16.8% (n. s.), respectively. The number of women without any professional activity was 8.8% and 6.8% (n. s.), respectively. The type of works is similar in both groups.

Conclusion: The presented Results are in contrast to earlier Results reporting that professional activity represents a risk factor for HDP. On this background the personal attitude towards a professional activity should be considered in any individual case.
Do hypertensive diseases in pregnancy have a negative influence on the postnatal partnership of the parents?

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Background: Hypertensive diseases in pregnancy (HDP) are a major challenge for the adaptation to parenthood. At the same time the quality of the relationship influences the long-term health of all family members. Therefore the study aimed to investigate satisfaction with partnership and separation after hypertensive disorders in pregnancy.

Methods: Self-administered questionnaires were sent to 2600 women with hypertensive diseases in pregnancy and to 1484 controls. 737 women with HDP and 624 control women matched for nationality, educational level and parity.

Results: Women having developed HDP were significantly less often satisfied with their partnership than control women (76%/81.1%; p<0.05). The number of women separating from the father of the index-pregnancy was not significantly different in both groups (1.22%/2.24%; n. s.).

Conclusion: Although the diagnosis if HDP is associated with specific stressors, the separation rate is not increased after such a pregnancy complication. Adapted peripartal psychosocial support may facilitate the start of family life.

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The correlation between adverse childhood experiences and hypertensive diseases in pregnancy

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Background: Although hypertensive diseases in pregnancy remain one of the leading causes of prematurity and fetal as well as maternal deaths current research has failed to develop a clear model of its aetiology. Psychosomatic counseling in women suffering from HDP has shown a positive history for sexual abuse in some of these women. It was the aim of the presented study to investigate whether women with HDP have particularly often experienced sexual abuse.

Methods: A self-administered questionnaire developed for the current study was completed by 142 women with HDP and 124 matched (age, nationality, education, parity) control women. The index-pregnancy in cases was defined as the first pregnancy conducted beyond the 24th gestational week which was complicated by HDP. Adverse childhood experienced were investigated using a modified version of the childhood trauma questionnaire (CTQ).

Results: Women developing HDP during their index-pregnancy reported significantly more often on sexual abuse experiences during childhood than controls (13.5%/ 3.6%, p =0.046). There was no significant difference with regard to physical abuse experiences in both groups.

Conclusion: Sexual abuse experiences should be considered as a risk factor for HDP.

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Recurrence risks of hypertensive diseases in pregnancy after HELLP syndrome – data from 148 women in Germany

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Background: Although the question on the recurrence risk of HELLP (Haemolysis Elevated Liver enzymes and Low Platelets) syndrome is very important for adequate counseling, scientific knowledge on this topic is scarce.

Methods: Data on subsequent pregnancies for 148 Caucasian primiparae with a diagnosis of HELLP syndrome in the index pregnancy and with at least one subsequent pregnancy going beyond 24 weeks’ gestation were analyzed to determine recurrence risk of hypertensive diseases in pregnancy. Recurrence risk was calculated with regard to disease severity in the index pregnancy.

Results: Among 148 pregnancies subsequent to HELLP syndrome 56.1% of the women were normotensive. The recurrence rate was 12.8% for HELLP syndrome, 16.2% for preeclampsia, and 14.2% for gestational hypertension only. Women with HELLP syndrome ≤32 gestational weeks tended to show a greater risk of complicated subsequent pregnancies compared to women presenting with HELLP syndrome after 32 gestational weeks.

Conclusions: Women with a diagnosis of HELLP syndrome are at a strongly increased risk of recurrent HELLP syndrome, preeclampsia or gestational hypertension, however currently no clinical or laboratory parameters allow to predict recurrence risk in any individual case.

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Pre- and postnatal emotional stressors in future parents with pre-eclampsia and HELLP-syndrome – an evaluation of psychosocial factors and their consequences on pregnancy course

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Background: A variety of specific stressors in hypertensive diseases in pregnancy (HDP) leads to the fact that these complications represent a major challenge to offer adequate somatic and psychosomatic support. It was the aim of the presented study to investigate the experience of women with HDP with different stressors following the diagnosis of the disease.

Methods: A questionnaire developed for the study was answered by 738 women with at least one HDP. Questions on specific stressors were developed from consultations with women suffering from HDP and from the clinical experience of the investigators.

Results: The three main stressors were fear regarding the health status of the child (307/41.6%), the duration of the hospital stay (97/57%) and a delivery by caesarean section (226/39%). Most stressors varied strongly with the gestational age at delivery. However, the type of HDP showed no correlation with different stressors. The main protective factor was the support provided by the medical staff and a short distance to the neonatal intensive care unit.

Conclusion: Diagnosis of HDP leads to important stress during pregnancy. Beside known stressors of any obstetrical complication women with HDP have to face sudden eventually life-threatening changes in the maternal and fetal health status. As stress may have an unfavorable influence on the development of HDP, these aspects should be considered in pre- and postnatal care.

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What is the recurrence risk after pre-eclampsia in Germany?

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Background: Data on the recurrence risk after hypertensive diseases in pregnancy (HDP) are central in counseling on future pregnancies. However, data available today rarely differentiate between different types of HDP. As ethnic backgrounds influence the incidence of HDP it remains unclear how strongly international data correlate with the situation in Germany.

Methods: To improve counseling data from 169 consecutive pregnancies in Caucasian women recruited in Germany after pre-eclampsia in the index pregnancy were analyzed. A severe pre-eclampsia was diagnosed with a hypertension $\geq 160/110$ mmHg after the 20th gestational week and a proteinuria $\geq 5$ g/L in 24h urine specimen or dip stick score $\geq 3+$.

Results: From the 169 consecutive pregnancies 41.4% were normotensive. A HELLP syndrome was diagnosed in 4.7%, a pre-eclampsia in 28.4% and gestational hypertension in 23.1% of the pregnancies. After the index-pregnancy 2.4% of the women developed chronic hypertension. Of the 158 women whose severity of HDP could clearly be identified 22% presented severe pre-eclampsia. In 94.3% of the women with mild and 60% of the women with severe pre-eclampsia HDP was diagnosed in the consecutive pregnancy ($p<0.0001$).

Conclusion: After pre-eclampsia the risk to develop another pre-eclampsia or gestational hypertension is increased significantly. However a severe compared to a mild pre-eclampsia in the index-pregnancy is not associated with a higher risk for another hypertensive complication during pregnancy.

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Maternal body mass index, smoking, and the somatic classification of neonates

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Background and aim: Smoking during pregnancy increases the risk of delivering a small-for-gestational-age (SGA) infant. Maternal obesity is associated with increased rates of large-for-gestational-age (LGA) infants. We aimed to investigate SGA and LGA rates in underweight, normal weight, and obese non-smoking women compared to smokers.

Material and methods: We analyzed data from the perinatal statistics of eight German federal states of 1998-2000 (n=508,926 singleton pregnancies). For the somatic classification of neonates we used the 10th and 90th birth weight percentiles calculated from our data.

Results: 16.1% of all pregnant women were smokers. In normal weight non-smokers (BMI=18.50–24.99) the SGA rate was 9.0% and the LGA rate was 8.4%; in normal weight smokers, the SGA rate was 19.4% and the LGA rate was 4.0%. In underweight non-smokers (BMI<18.50) the SGA rate was 16.0% and the LGA rate was 3.6%; in underweight smokers the SGA rate was 29.5% and the LGA rate was 1.5%. In obese non-smokers (BMI>29.99) the SGA rate was 6.1% and the LGA rate was 18.8%; in obese smokers the SGA rate was 12.0% and the LGA rate was 11.5%. In underweight women smoking increased the SGA rate by 13.5%. In obese women smoking decreased the LGA rate by 7.3%.

Conclusions: Smoking during pregnancy doubles the rate of SGA infants in both underweight and obese women. In obese women there was a reduction in the LGA rate with smoking. Smoking during pregnancy has a profound impact on neonatal outcome and needs to be a focus of interdisciplinary discussion.

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Diabetes mellitus of gestation and factors of danger

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Aim: The study it is the evaluation of factors of danger for the appearance of diabetes mellitus during the gestation.

Material-method: 1140 pregnant were submitted in screening test with 50gr glucose and 291 pregnant were submitted later in saccharemic curve with 100gr glucose for the investigation of diabetes mellitus during the gestation in the Gynecologic Clinic of Hospital of Pyrgos. In all was recorded age, familial background, indicator of mass of body, the number of childbirths.

Result: The effect of indicator of mass of body <20kg/m2 is low in the diabetes mellitus of gestation, the indicator of mass of body >25kg/m2 has statistically important effect in the diabetes mellitus of gestation. The effect of familial hereditary background is statistically important in the diabetes mellitus of gestation. The effect of age has statistically important effect in the diabetes mellitus of gestation. Pregnants that have >4 childbirths it statistically has effect in the diabetes mellitus of gestation.

Conclusion: The obesity with indicator of mass of body >25kg/m2, the familial hereditary background of diabetes mellitus and the age of gestation constitute important factors of danger of diabetes mellitus and the screening test with 50gr glucose are imposed in the pregnant women.

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Is repetition of screening important for gestational diabetes mellitus?

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Aims: Gestational diabetes mellitus (GDM) can be recognized by screening, because it has no signs. GDM is screened by a number of different methods. The goal of this study was the repetition of screening for GDM to be worth. Methods: 2260 women in Tolna County were followed through delivery. District nurses returned questionnaires from 2138(94.6%) women. The 75g OGTT was performed to screen for GDM in all pregnancies between 24-28 weeks according to WHO criteria. If the OGTT Result was negative, but fasting glucose level was between 6.0 and 7.0mmol/l and/or a postload glucose level between 6.8 and 7.8mmol/l, testing was recommended again within a month.

Results: Out of 2013 women, 173(8.6%) were diagnosed with GDM. (Repeat screening slightly increased GDM incidence). Diagnostic OGTT failed in 125 mothers (5.8%). Of the 2138, 216 were recommended for repeat screening, 43 of these were in the control examination and GDM was diagnosed in 6 of the 43. The incidence of GDM would have been 8.3% without repetition. If all of 216 women go to repetition, then probably 30 women would be GDM instead of 6. Thus the prevalence of GDM 9.9% would be instead of 8.6%.

Conclusions: This study shows that repeated testing Results in slightly higher incidence of GDM, but the outcome of pregnancies can be improved by recognizing some new cases of GDM. Authors recommend repetition of screening for GDM if the glucose levels are upper limit of normal range, and efforts should be made to encourage more gravids go for the repeated test.

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The Offspring of Pregnancy Induced Hypertension – a candidate to the metabolic syndrome

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Introduction: Pregnancy Induced Hypertension (PIH) is a common occurrence. Maternal, fetal and neonatal mortality and morbidity often a burden. What happens in the mid-long run?

Objectives: Evaluate: 1) Peri(neo)natal problems 2) Midterm outcome for the offspring

Methodology: Data collection from maternal and neonatal files and prospective clinical evaluation of the offspring at school entry.

Results: The incidence of PIH was 3.9%; of those, 61.7% developed pre-eclampsia, 4.8% HELLP. IUGR identified in 9.4%. Caesarean section 48.3%. No maternal or fetal deaths were recorded. Mean gestational age 38 weeks; birth weight 3169g, 20.8% being SGA; by Ponderal Indices only 9.1% were <10th centile. No neonatal deaths occurred and morbidities overlapped those of other babies, of similar GA.

Of the 351 neonates, 197 (66.1%) were available for follow-up at mean age of 67 months. Mean weight was on the 75th to 90th centile whilst BMI on the 85th to 90th. Mean systolic BP was >50th centile; dyastolic <50th. At first assessment 43/197 showed raised BP; of the 32/43 re-evaluated, 19% showed BP above the 95th centile.

Discussion: Neonatal morbidities were not significant, albeit 6.6% admissions to NICU. Ponderal indices, but not BW/GA, correlate to IUGR. At follow-up overweight was a feature. After re-assessment, 6/32 showed BP >95th, representing 3.8% of the total population, an under estimation due to failures.

Conclusion: The latter metabolic syndrome of adulthood renders these children a high risk group from childhood.

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Fetal growth in underweight pregnant women (BMI<18.50kg/m²)

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Aim: We aimed to examine the influence of maternal underweight status on fetal growth.

Material and methods: We analyzed data from the perinatal statistics of eight German federal states of 1998-2000; n=508,926 singleton pregnancies. Of these 19,824 women (4.0%) were underweight (BMI<18.50kg/m²) and 320,148 women (64.1%) were of normal weight (BMI 18.50-24.99kg/m²). For the somatic classification of neonates we used the 10th and 90th birth weight percentiles calculated from our data and adjusted for duration of pregnancy.

Results: Mean birth weight was lower in underweight compared to normal weight mothers, 3139g vs. 3360g. In very underweight women (BMI<16.50kg/m²) mean birth weight was even lower, 2984g. The rate of small-for-gestational-age (SGA) neonates increased from 10.3% in normal weight women to 18.7% in underweight women. The rate of large-for-gestational-age (LGA) neonates decreased from 7.9% in normal weight women to 3.2% in underweight women, and even reached 1.8% for very underweight women.

Conclusions: Underweight women are at high risk of experiencing fetal growth restriction. Therefore they need a high level of care already pre-conceptionally aimed at improving body weight. This is especially true for very underweight women.

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Multidimensional somatic classification of neonates according to maternal height and weight

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Background and Aim: In the somatic classification of neonates the problem arises that children born to relatively small and light mothers are too often classified as ‘small for gestational age’ (SGA) and children born to relatively tall and heavy mothers are too often classified as ‘large for gestational age’ (LGA). The reason for this is the use of a ‘one-size-fits-all’ classification scheme. Here we present standard values for the somatic classification of neonates adjusted according to maternal height and weight.

Material and Methods: We analyzed data of 2.3 million singleton pregnancies from German perinatal statistics (1995-2000). We calculated separate birth weight percentiles for 12 groups of women formed according to maternal height and weight. Birth weight percentiles (3rd, 10th, 50th, 90th, and 97th percentiles) were also adjusted for gestational age and calculated separately for boys and girls.

Results: Maternal height and weight have a profound impact on the somatic classification of neonates. Between different groups of women there were differences at the 10th birth weight percentile of up to 197g and 380g at 34 and 40 weeks’ gestation, respectively. At the 90th birth weight percentile the corresponding differences were up to 370g and 633g.

Conclusions: Maternal height and weight are important determinants of birth weight. We therefore recommend taking maternal height and weight - and not just duration of pregnancy and birth weight - into account when classifying neonates. Software for the somatic classification of neonates adjusted for maternal height and weight has been developed.

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Antenatal surveillance and outcome in fetal growth restriction

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Background: Evaluation of fetal growth is common obstetric practice. Fetal growth restriction (FGR) affects 15-25% of pregnancies and is associated with significant morbidity and mortality. Routine and selective ultrasound biometry can estimate fetal weight and predict growth restriction.

Patients and Methods: Retrospective analysis performed in 442 patients admitted in our ultrasound units between January/04 and December/07, with the following criteria: single pregnancy with fetal weight below the 10th centile for gestational age (Hadlock formula). Etiologic factors, gestational age at diagnosis and at birth, number of U/S examinations, mode of delivery and neonatal evaluation were the analyzed variables.

Results: Complete follow-up was possible in 392 patients. Mean gestational age at diagnosis and at delivery was 33 and 38 weeks, respectively. Vaginal delivery was performed in 209 babies (53.3%) and caesarean section in 183 (46.7%). Ninety-seven (24.1%) of 402 intrauterine growth-restricted fetuses were delivered before 37 weeks of gestation. Emergency caesarean sections performed for fetal distress occurred frequently. Mean birth weight was 2536g (from 410 to 3610g) including 161 neonates (41%) below the 10th percentile. There were 390 live births, one intrauterine death and one medical termination of pregnancy.

Conclusions: The goal of fetal surveillance in FGR is to balance fetal and neonatal risks to optimize the timing of delivery. In our data there was a poor correlation between ultrasound assessment of fetal growth restriction and birth-weight. Accurate FGR diagnosis is crucial for appropriate surveillance as well as for elective timing interventions.

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Comparison of neonates born to native German and Asian mothers with regard to their somatic development – an analysis of German perinatal statistics

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Aim: We aimed to investigate the somatic development of neonates whose mothers were classified in German perinatal statistics as originating from ‘Asia (without Middle Asia)’ compared to those born to native German mothers.

Material and methods: We analyzed data from the German perinatal statistics of 1998-2000; n=508,926 singleton pregnancies. Of these, 3,971 neonates were born to mothers from ‘Asia’ and 450,154 children were born to native German mothers. For the somatic classification of neonates we used the 10th, 50th, and 90th birth weight percentiles. We also calculated percentiles for the neonatal body dimensions for both groups of neonates.

Results: Mean birth weight was 3395g for infants of native German mothers, and 3277g for children of Asian mothers. Body dimensions also indicated that ‘Asian’ neonates were smaller. For body length the mean difference was 0.4cm (51.2cm vs. 50.8cm), and for head circumference it was 0.3cm (34.9cm vs. 34.6cm). Duration of pregnancy differed also: 62.6% of Asian mothers had a duration of pregnancy ≤39 weeks, compared to 50.9% of native German mothers. From 38 weeks’ gestation onwards the percentile curves for neonates of Asian mothers dropped off compared to German mothers.

Conclusions: Asian mothers on average have a shorter duration of pregnancy and their neonates are smaller compared to the native German population. It would appear that these two findings are linked. Neonates born to Asian mothers may need a different classification scheme with regard to somatic development than neonates born to native German mothers.

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Prematurity: A risk factor for the adult metabolic syndrome?

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Introduction: Small preterms are often a concern for psychomotor developmental outcome and neurosensorial sequelae. Are they also prone to the adult metabolic syndrome and, if so, how early does it start?

Objectives: To ascertain: 1) catch-up growth and deviations; 2) their correlation to gestational age (GA) and birth weight (BW).

Methodology: Data analysis from files of inborns, GA \( \geq 23 < 32 \) weeks, from January 1999 to December 2005. Statistic analysis by SPSS15.0.

Results: Out of 159 neonates 19 (12%) died before discharge; 29 transferred to local hospitals. Of the remaining, 103 children were available for assessment: GA 28.6±2.0 weeks BW 1,189.2±369.7g; 14 were SGA and 6 LGA. At 2 years corrected age all showed growth deceleration but by age 4 all started increasing centiles, a trend maintained at 6 years. This pattern, although not statistically significant, was more pronounced in those SGA. Subdividing the population into <26, 26-29, \( \geq 29 \) weeks, the same pattern was observed and similar Results were obtained when the cohort was classified according to BW at 250g intervals from 500 to >1,500g.

Discussion: Following an initial drop in weight, by the age of 2, all children showed catch-up by 4 years, sustained at age 6. Although these children cannot be considered obese or even overweight by standard parameters, they are, nevertheless, showing rapid weight gain especially those born SGA. These findings place these very preterm infants at risk for the later metabolic syndrome, whether of intrauterine or postnatal origins, but requiring tight follow-up.

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Pregnancy outcome in women of advanced age compared to younger women

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Introduction: The past decades have seen a remarkable shift in the demographics of childbearing worldwide. In Switzerland, the average age of primiparae has increased by 15 percent between 1971 and 2006. Women of advanced age are at higher risk for abortions, fetal aneuploidies, preterm deliveries, multiple gestations, gestational diabetes and preeclampsia. In this study, maternal and neonatal pregnancy outcome is compared between two age groups.

Material and methods: From 1.1.2003 to 31.12.2007 all births in women of ≥22+0 weeks of gestation aged ≥40 years (n=512) are included who are registered at University Hospital of Zurich. These are compared to patients aged 19 to 39 years (n=10088) regarding rate of caesarean sections, multiple gestations, preterm deliveries, preeclampsia including HELLP-syndrome and gestational diabetes.

Results: There is a higher rate of preterm deliveries: 24.4% vs. 17.2% (p<0.01), multiple gestations: 8.6% vs. 4.9% (p<0.01), caesarean sections: 62.3% vs. 38.5% (p<0.01), preeclampsia: 6.5% vs. 3.7% (p<0.01) and gestational diabetes: 6.8% vs. 3.0% (p<0.01) in the group of women aged ≥40 years. A logistic regression analysis revealed a strong association (p<0.001) between preterm birth and multiple gestations. Main risk factor for multiple gestations in a women over 40 are assisted reproductive technologies (p<0.001).

Conclusion: In women aged ≥40 years there are higher rates of multiple gestations, preterm deliveries, caesarean sections, preeclampsia and gestational diabetes. However, the overall outcome is also favourable in women of advanced age as 75% of them have born live infants at term.

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Effect of maternal age on perinatal outcome

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Background: The effect of advancing maternal age on infant outcome was examined to determine if there is a threshold for increased risk of adverse outcome.

Methods: In a retrospective cohort study, the outcome of 63,742 singleton pregnancies carried to 24 weeks or more and delivered in our hospital from January 1998 to June 2008 was reviewed, and infant outcomes were analyzed according to maternal age categorized into six groups as follows: <20 years (n=1,241), 20-24 years (n=8,392), 25-29 years (n=16,512), 30-34 years (n=17,172), 35-39 years (n=8,670), and ≥40 years (n=1,537).

Results: The incidence of preterm birth <34 weeks, small-for-age, and large-for-age, low birth-weight (<2,500g), and macrosomic (≥4,000g) infants were 2.8, 1.2, 1.4, 1.8, 2.6, and 3.6%; 14.7, 12.9, 11.3, 10.3, 9.8 and 10.9%; 13.1, 12.3, 14.3, 15.6, 17.9, and 17.8%; 9.4, 5.8, 5.0, 5.8, 7.0, and 8.2%; and 1.0, 2.6, 3.7, 4.0, 4.2, and 3.3% respectively (p<0.001 for all). There was no significant difference in the incidence of Apgar score <5 at the fifth minute (0.5, 0.6, 0.6, 0.7, 0.8, and 0.9% respectively) or perinatal mortality (0.6, 0.4, 0.3, 0.3, 0.4, and 0.4% respectively).

Discussion: Advancing maternal age had different effects on different perinatal outcomes without any apparent thresholds, and any arbitrary cutoff should be reappraised.

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The effects of regular exercises on pregnancy outcome

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Background: It has been reported that, in the absence of either medical or obstetric complications, 30 minutes or more of moderate exercise a day on most, if not all, days of the week is recommended for most pregnant women. Most women who report increased levels of physical activity are not at an increased risk of preterm delivery or reduced intrauterine growth. This study was conducted to look into the safety and effects of regular timed aerobic exercises during pregnancy on both the mother and the neonate.

Methods: Prospective, randomized, case-controlled trial study has been done on 120 healthy pregnant women in their first trimester. The data collected in Prenatal OPD care, Labor and delivery rooms of a university-based obstetrics department. After completing basic information forms, education on the specific exercises was given to each of them in 8 stages, which continued throughout the pregnancy. 63 patients that presented for delivery without any history of physical exercises were selected as control group.

Results: There was no significant difference between the two groups as regards their occupation. The exercising group experienced significantly decreased durations of labor. There was no significant difference in neonatal birth weight or Apgar scores. There were a significant decreased number of assisted deliveries in the exercising group.

Conclusion: Exercise during pregnancy shortens the duration of the second stage of labor, reduces the risk of assisted delivery and is safe for the neonate.

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Improving women's health and reducing feto-maternal mortality – towards the WHO millennium goals via intensified bilateral north-southern co-operation

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Eritrea has gained political independence after 30 years of armed conflict in 1993. Structures of public healthcare were destroyed. The MMR was 998/105 in 1995. The bilateral partnership between the Hammer Forum and the Orota referral hospital in Asmara started with the construction of a neonatology unit and the IOCCA. It was extended to obstetrical training both in Germany and in Asmara since 2005.

We evaluate key parameters in obstetrical care within a bilateral co-operation. The percentage of hospital deliveries remained stable at 30% for the last years. Deliveries increased continuously from 7549 (2004) to 8296 (2007). Stillbirth was 3.8% and 2.8% respectively. The rate of surviving LBW newborns increased from 681 to 839.

Curricula for midwives included training in AFM and introduction of improved management for PE women. The implementation of BP and proteinuria into antenatal care was completed by the introduction of iv magnesium and anti-hypertensive medication for severe PE. This considerably improved feto-maternal outcome within the Oroto hospital, the MMR reaching 46/105 in 2007. Regional differences within the country remain considerable.

Intensive co-operation between NGOs and central training and referral hospitals in developing countries based on mutual exchange is an effective tool to improve feto-maternal outcome. The mortality from hypertensive complications in pregnancy can be significantly reduced by training local personal. The next step will be the implementation of a specialization training in obstetrics and Gynecology for the first graduates of the Asmara Medical School thus opening a future perspective for improving women's health in Eritrea.

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Morbidity of obstetric patients admitted to the ICU of a tertiary hospital

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Introduction: Due to extremely low rates of maternal mortality in the modern medical setting, new indicators for the monitoring of maternal health have to be identified. Transfer to an intensive care unit (ICU) during pregnancy or puerperium has been established as such an indicator in recent publications dealing with near miss maternal morbidity.

Objective: The objective is to assess the causes of obstetric admissions to ICUs at the General Hospital of Vienna, Austria, and to evaluate the predictive ability of the APACHE II Scoring System in obstetric patients. Furthermore the most seriously affected patients and the factors most likely associated with severe morbidity are identified.

Methods: A retrospective chart review of obstetric patients who were admitted between the second trimester of pregnancy and 6 weeks post partum to an ICU of the General Hospital of Vienna, a tertiary care university hospital, between March 1996 and October 2001 as well as November 2004 and June 2009 is carried out.

Results: To this day (March 14th, 2009) 155 patients were included. The observed mortality rate amounts to 3.2% while the mean one calculated by the APACHE II Scoring system is 13.8%. A majority of patients (78.1%) is admitted for complications associated with pregnancy, the most common indications being (pre-)eclampsia and HELLP (31.2%) and major haemorrhage (33.7%).

Conclusions: The APACHE II Scoring system overestimates mortality in obstetric patients. Women suffering from puerperal sepsis had the poorest outcome. Complications associated with preeclampsia and postpartum haemorrhage account for the largest number of ICU-admissions.

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Critical illness in pregnancy. An overview of causes of admission and outcomes in an intensive care unit

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Objective: To describe pregnant and postpartum patients admitted at an obstetric intensive care unit (ICU), their diagnosis at admission, length of stay (LOS) in ICU and outcomes.

Methods: Retrospective analysis of demographic, diagnostic, LOS and outcomes until ICU discharge or death.

Results: We studied 245 patients admitted in the ICU of Maternidade Odete Valadares, Brazil, during the period 2007-2009. The mean age was 27.7±7.3 years; the mean gestational age was 31.6±7.2 weeks. Most causes of ICU admission were directly related to pregnancy (224 patients – 91%), while 20 patients (8%) were admitted by indirect causes. We divided the admission diagnoses in major groups: Hypertension diseases (116 patients - 47%), Hemorrhagic diseases (75 patients - 31%), Infections (46 patients -19%) and others (8 patients - 3%). The mortality rate and LOS in ICU of each of those groups was 2.5%, 3.8±6.3 days; 5.3%, 5.3±6.7 days; 6.5%, 7.7±8.8 days; 25%, 5.3±5.9 days, respectively. In 8 of 245 patients we could not include them in any of the first three groups (they were included in the group of other causes), 2 of these patients died, one had cardiac malformation, and the other one had sickle cell anemia.

Conclusion: In our obstetric ICU the mortality rate was 5%. The major cause of admission was hypertensive disorders, although the LOS in ICU and mortality rate of those patients was lower than the other causes of admission. The major morbidity and mortality was found in the group not directly related to pregnancy.

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Outcome of neonates transferred to a greek NICU during a three year period

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Introduction: Improvement in perinatal care is determined not only by advancements in the neonatal intensive care but also by improvements in the transportation of neonates to the NICU. The aim of the present study was to evaluate morbidity and mortality of neonates transported to one unit as well as to compare them to the inborn neonates.

Methods: Hospitalized neonates during the three year period (2006-2008) included inborns as well as neonates transferred to our unit from public, private nurseries and rural areas (islands and other municipalities). Neonates were classified according to the birth weight in 3 groups: A <1,500gr., B 1,500-2,500gr. and C >2,500gr. Outcome was assessed as low, moderate and severe morbidity (SM) and death (M) Serious morbidity included PVL, IVH grade 3 4, HIE and surgically corrected ROP.

Results: Increased severe morbidity (SM) and mortality (M) in neonates transferred from rural areas and especially in those with BW>2,500gr (table).

Conclusion: Morbidity and mortality is increased in neonates transferred from rural areas indicating the deficits in the transportation system and the significance of proper organization.

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Perinatal mortality: A quality indicator for perinatal care

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Introduction: Perinatal mortality rate is considered a quality indicator of health care. Clinical audit aims to identify errors or omissions in clinical practice and help in appropriate interventions to reduce avoidable perinatal deaths.

Objectives: This study was carried out to determine fetal outcome, and causes of fetal and early neonatal deaths.

Methodology: This retrospective study was conducted at a tertiary care hospital and included all the stillbirths, excluding medical termination of pregnancy, and early neonatal deaths between January and December 2008. Perinatal deaths were analyzed according to maternal characteristics, type of delivery and fetal characteristics, and classified according to Wigglesworth’s classification.

Results: Out of the 2699 total births in this period, 7 were stillbirths (SB) and 3 were early neonatal deaths (ENND). Out of the 7 SB, three were below 1000g in weight and of the 3 ENND, two were less than 1000g. Perinatal mortality rate was 2.6‰ and extended perinatal mortality rate (including stillbirth after 22 weeks or neonatal death before 28 completed days of life) was 3.7‰. According to Wigglesworth’s classification, 50% of perinatal deaths were in Group I, 20% in Group III, 20% in Group IV and 10% in Group V.

Discussion: Following regionalization of perinatal care in the mid eighties, in Portugal, perinatal mortality has been greatly reduced in double fingers to below 5‰ and, in our Institution, now stands at 2.6‰.

Conclusion: These outstanding Results substantiate the need and the worldwide obstetrics of rationalization of human and financial resources.

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Maternal mortality ratio in the province of Kütahya and the analysis of etiological factors; Turkey

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Aims: The aim of this study is to assess maternal mortality rate in the province of Kütahya and to analyze the etiological factors.

Methods: This population based study retrospectively analyzes 31 maternal deaths in Kütahya, from 1997 to 2008.

Results: In this time period, there were 81,557 live births and the maternal mortality ratio was found to be 38.01 per 100,000 live births. Information about reasons of 3 maternal deaths couldn’t be attained. The most common direct and indirect causes of maternal mortality were hypertensive disease of pregnancy (28.57%), infection (17.86%), obstructed labor (10.71%), uterin bleeding (10.71%), tromboemboli (10.71%) and cardiac diseases (10.71%). Most of maternal deaths were in the postpartum period (77.4%), pregnancies were near term (67.9%) and deliveries were by vaginal way (50.0%).

Majority of maternal death cases were from rural areas, in low socioeconomic status, graduated from primary school and reported to have antenatal care.

Overall 42.86% of all pregnancies ended with alive birth. 10.71% of babies died in early perinatal period, 32.14% of babies survived (still alive), 42.86% were intra uterin exitus, 14.29% were aborts. We couldn’t get any information from three mothers about their babies.

Conclusion: As most of the reasons of maternal mortality were preventable, improving antenatal care, socio economic status and education of mothers will help to decrease maternal mortality rate.

Key Words: maternal mortality, direct causes, indirect causes.

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Assessment of quality of hospital care for mothers and newborn babies in Albania

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The perinatal care assessment was carried out in three hospitals in Albania by WHO and Ministry of Health. Objectives were to: identify critical issues concerning quality of health care, suggest actions to improve quality at central and health facility levels, provide an opportunity for national team of assessors to familiarize with the assessment tools and methods.

The assessment was based on a tool developed by WHO, involved a multidisciplinary team of international and national professionals, included provision of a preliminary feedback to the local staff, and to MoH at the end.

The assessment showed that quality of care was in some cases good, but often substandard, in some cases poor: case management of most common conditions and complications doesn’t comply with international standards and evidence-based guidelines, integration and continuity of care is insufficient, important information for patients’ care is not available.

This situation, besides putting at risk health of mothers and babies, causes inefficient use of resources, unnecessary out-of-pocket payments, and may end with some real emergencies not to be dealt with promptly and appropriately.

Given the complex nature of the problems and their underlying determinants, the improvement requires a combination of action within health system reform. Immediate actions include technical support to guidelines development/dissemination, training in evidence-based medicine, effective perinatal care, clinical audit, development/adoptions of information/case management tools.

The assessment tools proved to be effective to guide the collection and analysis of key information regarding quality of care.

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Neonatal mortality in 2008 at Sousse (Tunisia) level III neonatology department

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Neonatal mortality has decreased by 50% in our department during last decades. Causes of neonatal death (ND) once dominated by prematurity and RDS are now changing.

Objective: mortality rate and causes of ND in 2008.

Methods: retrospective study of ND (<28d) in 2008.

Results: 118 ND/1777 (mortality rate =6.6%). Sex ratio =1.3. GA ≤28W in 31 NN (26.2%); 28-32 W in 39 NN (33%) and >37 W in 48 NN (35.5%). 89% were admitted immediately after birth. Antenatal corticoids were prescribed in 58% of NN[26 W-34W]. Causes of admission were mainly prematurity with RDS (n=47), malformation (n=27), severe hypoxic-ischemic encephalopathy (HIE)(n=14), RD in relation with materno-fetal infection (n=10) and suspicion of inherited errors of metabolism (IEM) (n=9).67% of NN died during first week. Causes of death were nosocomial infections (NI) in 31 NN, malformation in 27 NN, RDS-hemorrhagic syndrome (pulmonary or IVH) in 17 NN, HIE in 14 NN, IEM in 9 NN, MFI in 5 NN, preterm NN in 4 NN (24 W), chromosomal anomalies in 4 NN (2 T13,2 T18) and post natal infection in 3 NN. Other causes were BPD in 2 NN, hydrops fetalis in 1 NN and congenital nephrotic sd in 1 NN.

Although mortality due to early prematurity is decreasing, avoidable causes of NN mortality remain important represented by NI and hemorrhages in preterm NN accounting together for 40.6% of deaths. 26.2% of deaths were due to either malformations or chromosomal anomalies. Accurate prenatal diagnosis should detect them at an early stage in order to indicate pregnancy interruption. Prenatal monitorage and obstetrical-neonatal collaboration should prevent HIE representing 11.8% of deaths.

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Maternal mortality ratio (MMR) in Baghdad Teaching Hospital for the years 2006-2008

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Aim of the Study: This is a hospital based study aims to calculate the MMR in a tertiary hospital in Risafa District in Baghdad /IRAQ with a cached population of 3 millions for a period of 3 years.

Material and Methods: It is a facility based study. Data was collected from the questionnaires filled and sent voluntarily to the MCH dept. by the obstetricians who treated the women before death in hospital. These were analyzed to detect the cause of death, type of delivery, antenatal care status and age distribution.

Results: 24 maternal deaths were reported among 18760 hospital live births giving an MMR of 128/100 000 live births.

The leading direct causes of death were: bleeding 7/24 (29%), hypertensive disorders 6/24(25%), early pregnancy complications 5/24(21%), thromboembolism 2/24(8%), ruptured uterus 1/24 (4%).

Indirect causes of death were: heart disease 2/24(8%) and renal disease 1/24(4%). 12 deaths were referred from other hospitals.

12 /24 (50%) of deaths had no antenatal care.

The relative increase in deaths for 2008 is due to the relative increase in total number of annual deliveries and reporting the deaths in units other than the labor room and maternity ward, in addition to the increase in the number of unsafe abortions admitted for that year. (4 deaths).

Discussion and Conclusion: Avoidable factors make the majority of direct causes of deaths in terms of delayed referral to hospital, and timely action to treat the cause.

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Morbidity and mortality of extremely premature SGA infants of 26-28 wks of gestation in comparison to AGA infants of the same gestational age

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Introduction: Approximately 30% to 50% of extremely preterm neonates are SGA. Although there are conflicting published data, recent studies show an increased risk of complications related to prematurity in SGA infants compared with the AGA, including retinopathy of prematurity (ROP), severe intraventricular hemorrhage (IVH) and bronchopulmonary dysplasia (BPD). In addition, very low birth weight neonates who are SGA present higher mortality rates than their AGA counterparts.

Methods: Subjects consisted of 77 neonates of 26-28 weeks of gestation, 19 (24.6%) of whom were SGA. Data were analyzed using the SPSS 11.5 and the chi-square test.

Results: The mean GA and BW of SGA and AGA neonates were 27.5±0.5 weeks and 681±73gr compared to 27.6±0.5 weeks and 1,071±162gr respectively. The Results of the 2 groups are presented in the following table. Comparison of the two groups revealed an increased incidence of PDA, PH, sepsis, severe IVH and BPD in the SGA neonates (p<0.049, 0.013, 0.010, 0.048, and 0.001 respectively).

Conclusions: In this study, the extremely premature SGA neonates presented a higher incidence of BPD, PDA, PH, sepsis and severe IVH compared to the AGA group. There were no significant differences in the incidence of mortality, NEC and ROP. The excessive morbidity of the SGA group could be attributed to the unfavorable in utero environment.

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Respiratory support in premature babies – 32 weeks of gestation. 9 years experience

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Authors evaluated the evolution, from 2000 to 2008, of respiratory support and surfactant strategies, mortality and morbidity.

Retrospective study of inborn preterm infants ≤32 weeks, comparing two groups (year of birth 2000-2004 and 2005-2008), without major malformations/prenatal diseases. Data taken from medical records. Statistical analysis with SPSS 13.0. Significance: X2/U Man Whitney (p<0.05)

499 newborn were included.

Group 2000-2004 (224 NB):
Mean gestational age 28.54 (23-32) weeks; mean birth-weight 1141(430-2350) g; complete prenatal steroid course 64.3%.
Surfactant administration: 57% entubated and 13% insure strategy.
63.8% needed invasive ventilation (9.4%HFV), 24% only nCPAP. Mean duration of invasive ventilation 9.3 days. Pneumothorax 8.5%. Mortality 17.4%. Outcome of survivors: IVH (grade3/4) 7.6%; PVL 3.8%; ROP (≥2) 9.2%; oxygen at 28 days of life 24.9% (severe CLD 4.9% of survivors).

Group 2005-2008 (275 NB):
Mean gestational age 28.63 (23-32) weeks; mean birth-weight 1184(394-2290)g; complete prenatal steroids 72.4%. Surfactant administration: 45.8% entubated and 35% insure strategy.
48% needed invasive ventilation (12%HFV), 44.4% only NCPAP. Mean duration of ventilation 10 days. Pneumothorax 4.0%. Mortality 13.5%.
Outcome of survivors: IVH (grade3/4) 4.6%; PVL 4.2%; ROP (≥2) 14.4%; oxygen at 28 days of life 24.8% (severe CLD 2.5% of survivors).
Comparing the two groups: need for invasive ventilation, surfactant strategy, mortality and major morbidity (CLD only for severe forms) showed significant difference except for PVL. Mean duration of invasive ventilation did not change.
Respiratory support has changed towards nCPAP and insure strategy for surfactant administration. Mortality and major morbidity has been reduced.

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Strategies to reduce maternal mortality in developing countries

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MFCI and Hammer Forum as non-governmental organizations (NGOs) are committed to the reduction of maternal and perinatal mortality in Africa and support the Millennium Development Goals. Both NGOs also support the WHO’s Agenda 2020, which calls for an 50% reduction of maternal mortality (MM) by 2020 in Africa.

At the present time, the lifetime risk of dying during pregnancy is 1:16 in sub-saharan Africa (NEJM 356, 2007). There are more than 500,000 maternal deaths per year (WHO 2004), nearly half of these occurring in the African region.

The main causes of MM in developing countries are hemorrhage post partum (25% of death causes), unsafe abortion, septicaemia, eclampsia and HELLP syndrome, obstructed labor and/or uterine rupture, anaesthesiological complications, as well as three major delays:

- Delay in deciding to seek professional care
- Delay in reaching the facility
- Delay in receiving appropriate care after arrival at the facility

From our experiences, especially in Eritrea, the following strategies and steps seem to be able to make motherhood safer in developing countries:

1) Constructive and progressive policy dialogue on sexual and reproductive health
2) Concentration of high-risk pregnancy surveillance and obstetric care to secondary or even tertiary referral level
3) Postgraduate education and continuous training of health care workers on all levels.
4) Mobilizing financial resources and providing more money for maternal health (WHO; World Bank and other donors).
5) Avoidance of substandard care factors and of delays.
6) Registration and confidential enquiry of maternal deaths and intrauterine fetal deaths.

In Asmara, the capital of Eritrea, maternal and neonatal mortality has been significantly reduced in the referral hospital (Orotta Maternity) with more than 8,000 births per year. The next steps of the obstetrical and neonatology teams of Hammer Forum and MFCI in Eritrea will be proposed and discussed.

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Perinatal mortality in Mbale, eastern Uganda: a community based prospective cohort study

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Objective: Low and middle income countries account for 99% of the 4 million neonatal and 4 million stillbirths each year. Most of these deaths go unrecorded and only a few studies have been done on perinatal mortality in these countries. The objective of this study was to investigate perinatal mortality and determine its risk factors in Eastern Uganda.

Methodology: A community based prospective cohort study with 866 pregnant women was conducted between January 2006 and May 2008. The women were followed up till 6 months postpartum. Information was collected on socio-demographic factors, mother’s health behavior, delivery and fetal outcome. Relative risks for perinatal mortality risk factors were computed and logistic regression done to control for potential confounders.

Results: Overall perinatal mortality rate was 42/1000 pregnancies: 23% of the deaths were due to prematurity and 46% were associated with complicated deliveries. After controlling for potential confounders, nulliparous women had a higher risk for perinatal mortality (RR 3.8, CI 1.5, 9.8) as did women who delivered at home (RR 4.1, CI 1.8, 9.3). Compared to rural women, women in urban slums had a higher risk of losing their babies (RR 3.8, CI 1.6-8.8).

Conclusion: Most perinatal deaths occurred to women delivering at home, in urban slums and among nulliparous women. The common direct causes were prematurity and complicated deliveries. Efforts to reduce perinatal mortality should focus on improving delivery care at the facilities and prevention of prematurity. Urban slum dwellers should be considered a vulnerable group.

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Critical analysis of the rate of neonatal hospitalization in our hospital

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Objective: To analyze the newborn hospitalized during year 2007, to identify what were unnecessary in order to introduce possible improvements.

Material and methods: We examined all new born all hospitalized during 2007. We studied three diseases and the variables that justify the hospitalization: analytical with froits sanguineous and protein C reactive in mothers with intrapartum fever, pregnant with positive Streptococcus agalactiae without antibiotic or incomplete prophylaxis and premature rupture of membranes more than 24 hours.

Results: 70 hospitalizations of 526 newborn (13.3%). The causes were: 21 cases by high septic risk, neonatal jaundice in fototerapia level (19), new born with low weight (5), neonatal fever (4), premature (4), 3 hematological diseases (thrombocytopenic, neutropenia and son of mother with idiopático thrombocytopenic purpura), 3 with neonatal low Apgar, 3 by distres respiratory immediate to the birth, 3 hypoglucaemias, 1 pause of apnea, 1 difragmática hernia, 1 by extrasístoles and 1 by social cause.

Conclusions: The majority of neonatal hospitalization corresponds septic risk (30%) and hiperbilirrubinemia neonatal (27%). Although we are within the objective proposed to make early puerperal discharges (24-36 hours postpartum) and that could increase the rate of neonatal hospitalizations (new born with jaundice that remained more time in observation, hypoglucaemias for the lack of a adequate lactancia, new born preterms limit and new born at the risk of past infection that only requires new analytical determination 24 hours). On the other hand there is a certain interobservant variability in the reading of froits, as well as in the interpretation of the analytical Results.

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Normal childbirth care. Data information system

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Introduction: The quality of normal birth is a priority for the Department of Health in Catalonia. In the year 2005 two Catalan public hospitals started a pilot project offering natural care for normal birth. The project has been implemented progressively in many other hospitals. Due to the great success Catalonia has currently 12 hospitals offering these services. During this period of time, the Ministry of Health of Spain and The Department of Health in Catalonia have compromised to improve clinical practice and guaranteed the quality of care in this field. Our priority now is to analyze the process to assess how these services are delivered.

Objectives: To develop a data information system to hospitals activity on natural birth. As well as to know activity on natural birth and women’ satisfaction.

Methodology: In order to develop this data system the Department of Health created a specialist’s working group. This group was integrated by midwives and obstetricians that were working for these pilot hospitals. We also got the collaboration of the Iberoamericana Cochrane Collaboration Association: We will gather the data via web in different steps:

First: Collect women preferences (birth plan): To be completed by woman on herself or with professional support.

Second: Obstetric outcome and childbirth plan fulfillment (To be completed by professional after birth and at the hospital)

Third: Woman satisfaction degree. (To be completed by woman at home)

Results: Data information system has been developed and implemented in 5 pilot hospitals. We have developed a training course to show professionals how to use the Data information system. We expect to have some primary Results by January 2010

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Burden of major anomalies and their contribution to neonatal mortality

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Neonatal mortality (NM) accounts for about 70% of all deaths in the first year of life. Major anomalies (MA) remain as a leading contributor to NM.

Subjects and Methods: Our aim has been to evaluate the burden of MA as a prime cause of neonatal death (MAND) in the last 14 years in our maternity.

Results: Between 1995 and 2008 there were 35,688 livebirths (LB), 533 of them presented at least one MA, an incidence of 15/1000 LB. The overall NM was 111 cases (3.1/1000 LB) and 34 deaths (30.6%) were due to MA, a frequency of 6.3% of MAND among 533 neonates with MA. The mean ratio of MAND/1000LB was 1.02 (range 0.0 – 1.6). Many MAND were lethal, such as Potter’s sequence (6 cases) and major neural tube defects (3 cases). Heart malformations (7 cases), diaphragmatic hernia (4 cases), severe brain maldevelopment and chromosomal abnormalities (both 3 cases) and congenital muscular dystrophy (2 cases) were the most frequently found (73.5%). There were also a single case of lung lymphangiectasia, bladder extrophy, open bifid spine, fetal hydrops, yeyunal atresia, lycencephaly, and congenital hemochromatosis, in total 7 cases.

Conclusions: The overall incidence of MA was 15/1,000 LB and the rate among the 35,688 consecutive LB of MAND was 1.02/1,000 LB. The incidence of MAND among 533 LB who had MA was 6.3%. One third (30.6%) of all NM were due to MA. Further reduction of MAND depends heavily on early prenatal diagnosis and rapid skilful management postnatally.

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The clinical outcomes on fetal gastroschisis: Recent 10-year experiences in Asan Medical Center

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Objective: The aim of this study is to analyze the perinatal courses, fetal treatment and postnatal outcomes of fetal gastroschisis.

Methods: A retrospective review of the medical records of 35 cases (fetuses?) with a prenatal diagnosis of gastroschisis was conducted between March 1997 and April 2007.

Results: Twenty-eight fetuses were followed up and 17 fetuses of them were born alive. Chromosomal study was performed in 22 fetuses and no abnormality was detected in them. Associated anomalies except for gastrointestinal anomalies were found in 12 (34.2%) cases: amniotic band syndrome (n=8), scoliosis (n=6), cleft lip (n=1), hydrops (n=1), hydrocephalus (n=1), acrania (n=1). In 4 fetuses, amnioinfusion and amnioexchange were performed simultaneously for treatment. 4 cases (23.5%) were delivered by caesarean section. All neonates received corrected operation immediately after birth and 8 (47.1%) of them had postoperative complications. 3 were died and the overall survival rate was 82.4%. The average length of hospital stays for the survivors was 36 days (2~210 days).

Conclusion: Fetal gastroschisis diagnosed prenatally has a good prognosis and high survival rates. The Result of this study was not different from that of preexisting studies and will be a useful guide in counseling parents with a prenatal diagnosis of gastroschisis.

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Prevalence of congenital anomalies in Kütahya state hospital; Turkey

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Aims: To determine total prevalence rate, prevalence at birth, live-birth prevalence and distribution of congenital anomalies (CA).

Methods: In the hospital based study, during 2000-2008, registries of total 18422 births (live, still and terminated pregnancies) in Kütahya State Hospital were analyzed retrospectively. Total malformation prevalence, prevalence at birth and live-birth prevalence rate, malformation types, proportions of isolated and multiple anomalies were determined using ICD 10 and Euro CAT Guide 1.3. Distribution of CA by maternal age, settlement and baby's sex were determined.

Results: The sample consisted of 181 births with CA giving total prevalence of 98.25/10000 registered births. Live birth prevalence was 71.47/10000 live births. The proportion of all stillbirths with CA was 19.3% (35 stillbirths), termination of pregnancies due to CA was 9.4% (17 TOP), total live-born with CA was 71.3% (129); 18.6% of CA live-born babies (24 perinatal deaths) have died in early perinatal period. The proportion of isolated CA was 81.2% (147 isolated anomaly) and multiple anomalies were 18.8% (34 multiple anomaly). Totally 211 anomaly cases were registered. The most prevalent of CA was CNS anomalies 43.43/10000 births (37.91% of total anomalies) and neural tube defects prevalence was 36.91/10000 births (32.23% of total anomalies). No statistical correlation was determined between CA and maternal age (p>0.05), settlement (p>0.05) and babies sex (p>0.05).

Conclusion: CA registries should be collected and analyzed by health ministry nationwide to get prevalence of CA of the country.

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Prevalence of congenital heart defects in newborns in Germany: Results of the PAN study

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Objective: To investigate the current prevalence of congenital heart defects (CHD) in newborns in Germany and its relation to demographic and gestational factors.

Design: Prospective registration of newborns diagnosed with CHD. Data were provided by a total of 281 participating institutions.

Results: A total of 14,000 infants with CHD are presently recorded in the database. The CHD prevalence of the first birth cohort (07/2006 to 06/2007) was 1.08%. The most common lesions were ventricular septal defect (all types) (48.9%), followed by atrial septal defect (17.0%), valvular pulmonary stenoses (6.1%), persistent arterial ductus (4.3%) and aortic coarctation (3.6%). The most common cyanotic lesions were tetralogy of Fallot (2.5%) and D-transposition of the great arteries (2.2%). A single ventricle (all types) was identified in 2.8%, half of them being a hypoplastic left heart syndrome. Female gender was more common among mild CHD (57.3%), while male infants were observed more frequently among severe lesions (58.4%). In 53%, diagnosis was made within the first month of life. Prematurity and a birth weight below 2500g were about 3 times more common in infants with CHD than the national average of live births. The rate of CHD was doubled in multiple births.

Conclusion: The nationwide PAN study revealed a CHD prevalence in newborns in Germany of 1.08%. Haemodynamically insignificant cardiovascular lesions accounted for about two third of all defects. CHD was associated with prematurity, low birth weight and multiple births.

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Epidemiology and outcome of cleft lip and/or palate in Chinese infants: A 12 year study in a tertiary referral centre in Hong Kong

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Objective: The epidemiology of cleft lip and/or palate varies between different racial-groups, but data in Chinese infants is scarce. This study investigates the epidemiology and outcome of cleft lip and/or palate in Chinese infants.

Methods: This is retrospective study of Chinese infants in a tertiary centre from 1997-2008 with diagnosis of cleft lip and/or palate. Clinical characteristics and outcomes were reviewed.

Results: 197 infants were included in the study with male-to-female ratio 1.14:1. 3% (6/197) were delivered preterm. 24.3% (48/197) had cleft lip; 38.6% (76/197) had cleft palate and 37.1%(73/197) had cleft lip and palate. 10% (20/197) had syndromal diagnoses. Infants with syndromal cleft had significantly higher incidence of developmental delay (45% vs. 5%, p<0.005) and failure to thrive (40% vs. 1.7%, p<0.005). There were no major complications after cleft repair surgery. 10% required secondary surgical revision after initial lip repair to achieve better cosmesis. 15% required secondary palatoplasty for repair of palatal fistula. The incidence of velopharyngeal incompetence (VPI) was low (4.6% in our study vs. ~15% in the literature). The rate of antenatal diagnosis increased significantly in recent years (17% antenatal diagnosis established before 2006 vs. 40% after 2006, p<0.005).

Conclusion: Clinical characteristics and outcome of Chinese infants with cleft are similar to western countries, with a lower incidence of VPI compared to reports in the literature. Infants with syndromal clefts had significantly higher incidence of failure to thrive and developmental delay. Improved antenatal diagnosis in recent years will facilitate early counseling.

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High perinatal mortality rate among immigrants in Brussels, Belgium

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Objectives: Describe and measure inequalities in perinatal mortality according to maternal nationality and socio-economic status in Brussels.

Methods: This study is a population-based cohort study using the data from linked birth and death certificates from the Belgian civil registration system. Data are related to all babies born during the nine-year period 1998-2006 and whose mother was living in Brussels, irrespective of the place of delivery (137,974 newborns). Perinatal and post-perinatal mortality were analyzed according to the nationality and the socio-demographic characteristics of the mother at birth. We used logistic regression to estimate the odds ratios (ORs) for the association between mortality and nationality.

Results: Women of sub-Saharan Africa experience a 50% excess in perinatal mortality that mainly reflects a high rate of preterm deliveries, low birth weight and a low socio-economic level. Paradoxically, despite their favorable pregnancy outcomes, Maghrebians and Turkish experience a strong excess (50-70%) of perinatal mortality. Differences in age, parity distributions and multiple birth play no role, and the excess does not reflect low socio-economic level. This excess of perinatal mortality contrasts with the absence of excess of infant mortality.

Conclusion: In Brussels, patterns of inequalities in perinatal mortality vary according to nationality and perinatal mortality is increased in particular ethnic groups independently of the socioeconomic status. We suggest that suboptimal care and low access to care may contribute to differences in perinatal mortality among nationalities.

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Neonatal nosocomial sepsis in a level III intensive care unit – aetiology and antimicrobial susceptibilities

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Despite advances in supportive care and antibiotic use, nosocomial infection remains an important cause of morbidity and mortality in neonatal intensive care units (NICU), reason why the incidence and aetiology of nosocomial sepsis (NS) and antimicrobial susceptibilities of causative agents isolated in blood cultures remains a concern.

Retrospective chart review of newborns with NS admitted to a tertiary hospital NICU during 2007. Data on gestational age (GA), birth weight (BW), central venous catheter (CVC) usage, length of hospital stay (LHS), blood proven NS aetiology and its antimicrobial susceptibilities were collected. 402 newborns were admitted and 42 had NS (10.4%). Of these (60% surgical patients and 33% with congenital cardiopathy; median GA: 33 weeks; median BW: 1880g), 67% needed CVC during an average of 26 days. Mean LHS was 35 days. Coagulase-negative staphylococci (81%), Staphylococcus aureus (10%), Enterococcus faecalis (4%), Klebsiella ornithinolytica (4%), Candida spp (3%) and Escherichia coli (3%) were the most commonly isolated micro-organisms in blood (n=105). 93% coagulase-negative staphylococci and 70% St aureus were oxacillin resistant. All gram-positive micro-organisms were vancomycin sensitive. Most gram-negatives were β-lactams-resistant; all revealed carbapenems, quinolones and aminoglycosides sensitive. Five newborns died.

The high incidence of NS in our NICU may be explained by the severity of comorbidities and long LHS. Despite a continuous effort in pursuing asepsis the majority of causative agents identified are common skin and fluids contaminants. The knowledge of the microbial spectrum and its resistance pattern in each centre plays the most important role in the establishment of empiric therapy.

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Epidemiology of Necrotizing Enterocolitis (NEC) in our Neonatal intensive care unit

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Introduction: NEC, the most common surgical emergency in the neonatal intensive care unit (NICU) remains a health concern despite advances of neonatal care. The incidence of NEC is increasing with improved survival rates for small premature infants and varies between hospitals and also within the same institution in different periods. The purpose of this study is to investigate the influence of various factors over the value of incidence, mortality and survival period for the newborns with NEC in our nursery.

Methods and results: We performed a retrospective study over a period of 8 years (January 2000 to January 2008). The incidence of NEC in our NICU had an average value of 6.81% (78 cases out of 1145 admissions) with yearly values which varied between 4.64% and 10.06%.

The specific mortality had an average value of 8.58%. Yearly mortality values varied between 0 and 13.64% and were significantly (p<0.05) influenced by: gestational age, birth weight, Apgar score, disease stage, intestinal lesions of necrosis and perforations, need for surgical intervention, septic and surgical complications.

Also, our patient’s survival period during hospitalization was significantly (p<0.05) influenced by the presence of oliguria and/or hypotension at the admission moment and the length and severity of intestinal lesions.

Conclusions: NEC remains a challenging disease for all the investigators. In this regard we have to improve our understanding of the disease process and develop better strategies for prevention and treatment.

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Incidence and outcome of necrotizing enterocolitis in a neonatal intensive care unit

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Introduction: NEC is the most frequent gastrointestinal neonatal problem related to serious morbidity and mortality in the NICU. Prematurity is considered the most important causative factor.

Purpose: To study the incidence of NEC in our department during a two-year period.

Materials and Methods: Neonates with definite NEC were included in this study over a two-year period. They were divided into three groups according to their gestational age (GA): Group A, (GA<32w); Group B, (GA 32-37w); Group C, (GA >37w).

Results: In the group A (n=6), the age at onset of disease was 10.33±6.28 days. The clinical situation was serious associated with abdominal distension, grossly bloody stools. Increased C-reactive protein, leukocytosis, thrombocytopenia were present. All neonates sustained operation. Mortality was high (33%).

In the other two groups (B, n=12; C, n=2), the age at onset was 5.07±3.85 days. The main clinical symptoms were abdominal distension, grossly bloody stools (12 out of 14), bilious emesis (4 out of 14). Laboratory studies were moderately deteriorated in some neonates (9 out of 14). Feeding was initiated at 1.74±0.825 days (maternal milk was given in one neonate). 8 out of 14 neonates were operated on. Mortality rate was 0%.

Conclusions: NEC occurs in both premature and full term neonates. However, is more serious in the premature population related probably to its gastrointestinal tract immaturity. Apparently more mature neonates have better prognosis.

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Does neonatal sepsis have a protective role on the development of allergic diseases on childhood?

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Background: The neonatal sepsis is the most important cause of neonatal deaths in the community, accounting for over half of them. Allergy has an incidence higher than 20% in USA and between 10% and 20% in Europe. Allergic atopic disorders, such as rhinitis, asthma, and atopic dermatitis, are the result of a systemic inflammatory reaction triggered by type 2 T helper (Th2) cell-mediated immune responses against antigens (allergens) of complex genetic and environmental origin. A number of epidemiological studies have suggested that the increase in the prevalence of allergic disorders that has occurred over the past few decades is attributable to a reduced microbial burden during childhood, as a consequence of Westernized lifestyle (the 'hygiene hypothesis').

Aims: Value the role of the neonatal sepsis in the prevention of allergic diseases.

Methods: Retrospective study over ten years (1997-2006) of 216 newborns hospitalized on NICU for neonatal sepsis. 163 (75.5%) are survivor and a questionnaire has been proposed to their parents to investigate the subsequent development of allergic disorders in children.

Results: The collaboration of parents at the answers has been very positive (82.2%). 7% of 134 children developed allergic diseases until April 2008. 4 children (3%) presented atopic dermatitis, 2 (1.5%) drug allergy, 3 (2.25%) asthma and 1 (0.75%) alimentary allergy and asthma.

Conclusion: The hypothesis about protective role of neonatal sepsis on the development of allergic diseases on childhood seems to be confirmed by Results of our study. Future studies are necessary to support these dates.

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Multiple pregnancy. Incidence and management; our data

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The number of multiple pregnancies has increased – currently there is a frequency of 2.2% in our country.

Objectives: To evaluate the role of the multiple pregnancy in the neonatal outcome and to obtain a potential scheme for the unified treatment in our country.

Method: This is a retrospective study, period January 2004-December 2008. The study outlines 422 cases of treated multiple pregnancy.

Results: From the 422 cases studied, 409 (97%) of them were twin pregnancies, 3% of them were higher order. Preeclampsia is the most frequent with 12% of the cases. Birth has been attained in 11% of the cases in the period of 28 – 32 weeks, in 38% of the cases in the period of 33 – 37 weeks and in 51% of the cases at a pregnancy age of more than 37 weeks. This has been made in 56% of the cases by s.cezarea. In 9% of the cases the pregnancies have been induced ones and in 5% of the cases FIV. In 8% of the cases, it has resulted in fetal death in utero and in 13% of the cases there has been neonatal deaths. In 19% of the cases there have been differences in apgar score of 1 – 3 points.

Conclusions: It is noted an increase in the number of the induced pregnancies and FIV. Also, it is noted a significant improvement in the ecographic diagnostication and evaluation of these pregnancies. The obstetric treatment and care deserves appreciation.

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Congenital anomalies in twin gestations

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Objectives: The aim of this study was to set up the prevalence of congenital anomalies in twin gestations, to compare it among monochorionic and bichorionic twin pairs and range the anomalies according to their frequency.

Methods: Retrospective case control study which included 741 twin deliveries in the period from January 1st, 2000 and December 31st, 2008. Results: Among 688 twin pairs with known chorionicity 137 were monochorionic and 551 bichorionic. 6.8% of the monochorionic were with present congenital anomaly of one or both newborns which was almost twofold larger that the prevalence of congenital anomalies in bichorionic twins 3.7%. There was an increased rate of congenital anomalies for all major types of anomalies, except chromosomal abnormalities. We found cardiovascular, alimentary and central nervous system anomalies to be present in 73.5% of our investigated material. They were followed by musculoskeletal and urinary system anomalies.

Conclusions: Monochorionic twins, have a higher risk of congenital anomalies than bichorionic. The most frequent are cardiovascular, alimentary and central nervous system anomalies.

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Chorionicity in twin gestations and the risk of stillbirth

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Objective: To reveal the correlation between the chorionicity in twin gestations and the risk of stillbirth.

Methods: A retrospective cohort study comprised all cases of twin gestations of at least 24 weeks at University Clinic of Ob/Gyn in Skopje from January 1st, 2000 to December 31st, 2008. The risk of fetal death with advancing gestation was estimated for monochorionic-diamniotic twins and dichorionic-diamniotic twins. Twins with considered growth abnormalities, malformations or twin-twin transfusion syndrome were excluded from the study. Stillbirths according to the chorionicity were analyzed within these apparently normal gestations.

Results: Data from 688 twin pairs (137 monochorionic-diamniotic and 551 dichorionic-diamniotic twins) were calculated. Stillbirths occurred in 7 (5.1%) monochorionic-diamniotic and 9 (1.6%) dichorionic-diamniotic twin pairs. Monochorionic-diamniotic twins are at a higher risk of stillbirth in comparison with dichorionic-diamniotic twins. The risk of stillbirth is independent of gestation age after 24 weeks.

Conclusion: Monochorionicity increases the probability of adverse prenatal outcome, even among monochorionic-diamniotic twins without abnormalities.

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The obstetric outcomes of single fetal demise in twin pregnancy

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Introduction: Single intrauterine death (IUFD) complicates %0.5-6.8 of pregnancies during the second and third trimester. IUFD of one twin can result in poor outcomes for both monochorionic and dichorionic surviving co-twins. We presented the obstetric outcomes of single IUFD in twin pregnancies in a tertiary centre in which 20886 deliveries were performed in 2008.

Methods: 18 pregnant women with a diagnosis of single IUFD between April and December 2008 were included prospectively to determine the obstetric outcome. Since some patients were referred relatively at a later gestational week, only in 10 patients, chorionicity could be established. (7 didi twin, 1 diamniotic monochorionic, 1 monomono, 1 diamniotic; chorionicity was not clear) Mean maternal age was 28.3 (17-40). 7 of the twin pregnancies were due to ART. Others were spontaneous twin pregnancies.

Results: Mean gestational week at the delivery was 35.7. One pregnancy was terminated due to membrane breaking one week after the IUFD of the co-twin in 13th week. Mean single IUFD week of cotwin was 20.5 (7-36). Preterm birth complicates 9 out of 17 (%52, 9) of the patients. One of the iatrogenic preterm delivery was result of the intractable maternal hypertension. Presentation anomaly rate was %35.2 (6 out of 17). 5 of them were breech presentation (%29.4). None of the patients had impaired coagulation profile at the time of birth.

Discussion: A single IUFD in twin gestation occurs infrequently. Since complications are increased, a maternal fetal medicine specialist consultation and management at a tertiary centre might be warranted.

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Pregnancy at both ends of reproductive spectrum
1 year retrospective study

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Introduction: While teenage pregnancy rate is a Result of many factors, including a subculture in which there is a glorification of sexual activity without education of young people regarding its consequences, the elderly may have suffered from infertility; waited for an ideal moment, or simply did not use effective contraception.

Methods: Retrospective analysis of clinical files from pregnant with ≤17 years and ≥40 years, followed in the High Risk Pregnancy Appointment of the Hospital of Faro, from January to December 2008.

Results: In 2008 our hospital had 3125 deliveries, 47 of teenagers and 70 on women ≥40 years. On our Appointment we followed 65 teenagers and 30 of the elderly pregnant.

In relation to the teenagers, their average age was 16 years old; studied until the 7th grade; came from nuclear families where half of the mothers had been pregnant during adolescence; only 28% used any contraception and most of them had vaginal deliveries at term, without complications.

The elderly pregnant were in average 42 years and most had previous pathology or complications during pregnancy. The majority had a vaginal delivery at term.

Conclusions: Even though is known that teenagers are more likely to have growth-restricted infants, preterm labor and higher infant mortality, we do not came to those Results. What we notice is a delay between intercourse and initiation of contraception, being counseling essential.

The elderly gravida, as expected, had more previous pathology and more obstetrical complications.

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Unexplained infertility

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Abstract: Broadly speaking about 20% to 25% unfortunate couples belongs to group of unexplained infertility. Nearly 100 million couples are infertile world wide of which 20 to 25 million are from the unexplained group. We categories the infertile couples into -

1. Single defect in one partner
2. Single / multiple defects to one or both partners
3. No defect in either partner

The incidence of unexplained infertility will obviously depend on the extant of investigations of both husband & wife. Unfortunately this is possible in a particular setup. With additional investigation - incidence of unexplained infertility can be reduced 4% to 5% from higher rate.

It is surprising as to why sexually active couples remain infertile in spite of repeated attempting to conceive for at least 1-2 years. Using cumulative life style table projection on the observed pregnancy rate in the untreated presumably discouraged group - it has been observed that a couple with primary unexplained infertility has a 35% to 40% chance of conceiving over a 5-7 year period. None the less their infertility rate is significantly higher than in the population as a whole.

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Infertility treatment (IT) has been utilized consistently in the past two decades in Germany. We examine the characteristics of women who receive IT and the risks associated with successful IT-pregnancies in the 1990ies and in the current decade. The database is routinely collected perinatal data from the federal state Lower Saxony, Germany covering the years 1990-1999 (n=742,031) and 2001-2007 (n=456,372). It includes all live-births and stillbirths from 500 grams. In the 1990ies 2.9% and from 2001-2007 2.8% of all pregnancies in the registry were accompanied by IT. While professionals and housewives were the occupational groups most often using IT in the 1990ies, recently white collar employees became the largest group. Compared to non-IT pregnancies, among singletons conceived with IT, from 1990-1999 the risk for low birth weight (<2,500 grams) was OR=1.56 (95%-KI=1.47-1.65) and in 2001-2007 it was OR=1.56 (95%-KI=1.45-1.67), for multiples it was OR=1.69 (95%-KI=1.57-1.82) and OR=1.53 (95%-KI=1.42-1.66) respectively. The risk for neonatal mortality among singletons was OR=1.49 (95%-KI=1.09-2.04) in 1990-1999 and OR=1.87 (95%-KI=1.24-2.81) in 2001-2007, for multiples the risks were OR=1.58 (95%-KI=1.20-2.09) and OR=2.36 (95%-KI=1.72-3.23) respectively. Referring to low birth weight, adjustment for maternal age, occupational status, partner status, nationality and smoking always resulted in decreased but not diminished associations. Referring to neonatal mortality, in 2001-2007, adjustment for confounders resulted in non significant associations in singletons and in stronger associations in multiples. Further studies should examine the role that higher order multiples play for this Result. Women should be informed adequately about the potential benefits and risks of IT.

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Influence of weather, seasonality and lunar cycle on the incidence of spontaneous abortions: A retrospective study

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Background: There is poor and discordant literature about the influence of lunar cycle or climatic conditions on pregnancy outcomes. Our study aims to determine whether particular astronomic and meteorological conditions have any influence on spontaneous abortions.

Methods: We collected data about women hospitalized in our clinic for miscarriage between 2004 and 2008, and investigated moon features (Naples Observatory) and climatic conditions (OSMER Database) on the abortion date. Days were divided by abortions incidence, considering great an incidence major than the 3rd quartile of the data distribution. Data were analyzed by R (version 2.8.0), considering significant p<0.05. Also multivariate analysis was performed.

Results: Considered abortions are 2290. Apparently there is no lunar or climatic parameter statistically influencing abortions incidence but, considering only urgent recoveries for abortion, an higher incidence correlates with lower distance Moon-Earth (p<0.05) and phases of empty-moon (p<0.05) and last-quarter (p0.056). By multivariate analysis, higher miscarriages incidence Results influenced by low Moon-Earth distance, but not by moon illumination, which represent lunar phase.

Conclusion: Greater abortions incidence seems to be influenced by lower distance Moon-Earth (p<0.05) and empty-moon phase (p<0.05), but is probably due to a more complex interaction of various environmental and maternal conditions, and obviously embryonic inherited anomalies.

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Neonatal brain scanning: Does it correlate to late clinical outcome in preterm babies?

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Introduction: Neonatal ultrasound scanning (NUS) is routinely done in preterms. What’s the correlation to quality of survival?

Objectives: Correlate clinical outcome in childhood with NUS and whether NUS and Magnetic Resonance Imaging (MRI) findings are concordant.

Methods: File’s data from all inborns, gestational ages ≥23<32 weeks, admitted to NICU between January 1999-December 2005. Statistic analysis by SPSS 15.0.

Results: Out of 159 neonates, 19 (12%) died before discharge, 29 transferred to local hospitals. Of the 111 available children all attended follow-up. All had NUS, with abnormalities in 33 (30%): subependimary haemorrhage 70%; intraventricular haemorrhage (IVH) 24%; periventricular leukomalacia (PVL) 9%; ventricular dilatation 3%. Of these 33 children only 3 had severe impairment; the remaining 91% were clinically normal or had minor psychomotor developmental (PMD) delay, whilst of the 78 with normal NUS, one presented with Cerebral Palsy (CP).

MRI was performed in 17/33 with NUS abnormalities; although all were abnormal, findings were quite discordant: PVL, 9% in NUS vs. 82% on MRI. However, 82% of the children with abnormal MRI were either normal or had mild PMD delay. Conversely, of the 78 children with normal NUS, 14 were submitted to MRI revealing abnormalities in 11, one in a child with CP; the other children were either normal or with mild PMD delay.

Discussion: Abnormal NUS findings in neonates, unless severe, bear poor correlation to neurological outcome. MRI in clinically normal children with normal NUS adds very little information. However, normal NUS do not reassure for intact survival and MRI might be more sensitive in predicting outcome in these children.

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Urinary incontinence in nulliparous women: Incidence and associated risk factors

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Urinary incontinence (UI) is a common condition in pregnancy. Few studies have examined prevalence of urinary symptoms in nulliparous women before pregnancy.

Aims: To investigate the prevalence and incidence of urinary incontinence (UI) during pregnancy and examine risk factors for pre-pregnancy incontinence and incident cases in pregnancy.

Methods: The Maternal Health Study is a multi-centre prospective pregnancy cohort study. 1507 nulliparous women ≤24 weeks’ gestation were recruited by mailed invitation, with a response fraction of 21%. Participants completed a questionnaire at enrolment and telephone interview at 30-32 weeks gestation, with further follow-up to 18 months postpartum. Standardized measures were used to assess frequency and severity of UI.

Results: Prevalence of UI increased from 10.8% in the 12 months before the index pregnancy to 55.9% in the third trimester. UI before pregnancy was associated with childhood enuresis (Adj OR =2.4, 95% CI 1.6-3.4), higher pre-pregnant maternal BMI (AdjOR =2.3, 95% CI 1.4-3.8) and ≥1 previous miscarriages/terminations (AdjOR =1.6, 95% CI 1.1-2.3). The strongest predictor of onset of UI during pregnancy was occasional leakage (<once per month) before pregnancy (AdjOR =3.6, 95% CI 2.8-4.7).

Conclusion: The low initial response fraction necessitates some caution interpreting prevalence estimates, but is unlikely to compromise validity of analyzes assessing risk factors. The complex interplay of pre-pregnancy factors, pregnancy itself, and birth events in the aetiology of postpartum urinary incontinence requires further elucidation to inform primary and secondary intervention strategies.

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Epidemiology of breastfeeding in an urban population in Athens

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Introduction: The biology of human breast milk and the policy of encouraging breastfeeding, continue to be the object of much scientific inquiry. Despite the benefits of lactation for both mothers and infants, rates of breastfeeding remain suboptimal. This study was conducted to evaluate the rate and duration of breastfeeding in women who had given birth in General University Hospital “ATTIKON”, in Athens, between January and May 2008.

Materials and methods: A cohort of 248 women who had birth in “ATTIKON” Hospital was recruited to study their infant feeding practices. Breastfeeding education during pregnancy was offered to most of these women, in our hospital. All mothers were interviewed in hospital, the first days after delivery, and again in 1, 2, 3 and 4 months postpartum.

Results: The results showed that 90% of the mothers started breastfeeding immediately after delivery (60% exclusively). One month after leaving hospital 85% of the mothers continued breastfeeding (57.75% exclusively). Two months after delivery 70% of all women continued breastfeeding (53.77% exclusively). Three months postpartum, 60% of women continued breastfeeding (49.66% exclusively), while at the fourth month, there has been observed a further decline and the rate was 44.2% (30.9% exclusively). The main reasons given for discontinuing breastfeeding related to experiencing problems with the method of breastfeeding, anxiety over the sufficiency of milk supply and return to work.

Conclusions: The rate of breastfeeding in “ATTIKON” Hospital is higher than in other hospitals in Greece, because of the breastfeeding education during pregnancy. However, evidence-based interventions to promote breastfeeding need to be implemented.

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Obstetric factors associated with placenta accreta development in women with placenta previa

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Objective: To analyze obstetric factors predictive of placenta previa accreta development among population of pregnant women with placenta previa.

Methods: This was a 10 year retrospective case-control study of all cases of placenta previa conducted at University of Zagreb Medical School between 1992-2002.

Results: There were 202 cases of placenta previa (0.4%). Of those 14 (6.93%) were various degrees of placenta accreta. Obstetric factors significantly associated with placenta accreta development were history of previous caesarean section (35.7% vs. 8.0%, p<0.01, OR 6.41 (1.62-24.83) and complete placenta previa (71.4% vs.29.8%, p<0.01, OR 5.89 (1.61-23.42). Increasing number of previous caesarean section did not significantly increase the risk for placenta accreta development. Obstetric factors like advanced maternal age >34 years, history of previous abortion and anterior location of placenta previa did not significantly increase the risk of placenta previa accreta.

On the other hand complete placenta previa was found to be independently associated with placenta accreta development even after controlling for multiple confounding factors in multiple logistic regression analysis (Adjusted OR 3.75 (1.11-12.68), p<0.05).

Conclusion: Obstetric factors important for placenta accreta development in women with placenta previa are complete degree of placenta previa and history of previous caesarean section.

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Theoretical possibilities of umbilical cord blood autotransfusion in hungarian neonatal practice

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Background: Transfusion-need inversely proportional to birth weight. Volume of allogenic transfusions and number of donors have decreased over last decades. Nevertheless, these infants are exposed to the risks of allogenic transfusion. Autologous umbilical cord blood transfusion (UCBT) may reduce these complications but the method has not been spread in Europe.

Objective: To assess the potential use of UCBT in a Hungarian institution.

Patients and Methods: We have reviewed records of transfused newborns (n=164) in our Department between 2004-2005. We have assessed maternal l+ fetal morbidity, course of birth, perinatal events, maternal + neonatal blood group, laboratory values, nursing events and transfusion data in separate birth weight categories.

Results: Analysis of our data demonstrates the following: (1) Transfusion rate increases with lowering of birth weight. (2) In parallel, the number of donors and the relative volume of transfused blood also increases with lowering of birth weight; while the absolute volume is nearly the same. (3) In terms of collection, storage and volume of umbilical cord blood all examined newborns are potential candidates for UCBT. (4) For newborns <1,000g the half of the volume of allogenic transfusions could be substituted by UCBT; while for newborns >1,000g the entire amount of allogenic transfusion could be substituted by UCBT.

Summary and Conclusions: According to the literature, newborns of lower birth weight are more likely to receive transfusions. UCBT potentially could offer an alternative, in selected groups of patients. However, further examinations are needed in terms of technical and financial feasibility.

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Abstract: Tubal Hydration is an noninvasive method to reduce the tubal block or tubal spasm. Nearly 25% unfortunate couples are childless due to tubal block. Currently the following two methods like IVF & ICSI are being need for the treatment of infertile couples. These methods are completely invasive, costly & temporary. Economically mid level country like Bangladesh cannot afford this luxury procedure. More over socio religion factors are working against these. The most common causes of tubal blocked are M. R (repeated), D/C, unsafe delivery, ligation etc. Moreover the percentage of tubal blocks is rising faster. Considering all those ITRC is working with tubal hydration since- 2001. We found that pregnancy rate with take home baby is quiet encouraging. To my opinion tubal hydration practice should be one of the options treatments of tubal block. More and more study is needed.

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Smoke free pregnancy in Catalonia (Spain): Assessment of the results

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Introduction: The Health Department of Catalonia began in late 2006 introduction of smoke-free pregnancy. It is based on a structured intervention by professionals in relevant maternal and child health from a gender perspective. It includes specific training for professionals, specialized professionals and support for user intervention at all Catalonia and evaluation of outcomes in a sample of primary health centers.

Objective: Analyze Results of program evaluation

Method: Descriptive study. Structured interview to 458 pregnant smokers attending 18 primary health centers of different socio-demographic characteristics at first visit and in the third trimester. Include sociodemographic variables, history and pattern of consumption, smoking and passive partner, intention to quit smoking and using nicotine replacement therapy (NRT)

Results: Women smoked an average of 14.5 cigarettes a day at the time of pregnancy, 7.9 in their first obstetric and 5.6 in the third quarter. 64% of pregnant women who meet the predetermined criteria NRT starts. The prevalence of smokers in the third quarter was 77.8% versus 89.3% in the first visit. 74.9% of women are smoking partner and 52.8% say they are routinely exposed to environmental smoke snuff.

Conclusions: 22.2% of women quit smoking during pregnancy, 12.9% of control after the first pregnancy. Among those that did not stop there was a significant reduction in consumption during pregnancy. Most also have smoking

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Social and environmental influences in teenage voluntary abortions

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In 1990 in Romania about 1 million voluntary abortions were performed in Romania. That figure decreased steadily at about 100,000 in 2007. The rate of abortions among teenage girls increased meanwhile. The study’s main objective was to determine the main factors- social, familial, cultural, educational involved in the teenage abortion in our unit. We performed a study on 112 women who addressed to our unit requesting voluntary abortions in a period of 12 months. We used a questionnaire with 12 questions most of them related to familial, social, educational and religious issues that determined the resolution to solicit abortion. 39% of the women soliciting abortions in our unit were teenage girls. The profile of such a girl is: urban background, enrolled in college or with primary studies, unmarried, low family income, orthodox. The main reason for requesting abortion was the fear of family reprimand, unknown father (multiple sexual partners or occasional sexual intercourse), poverty or already other children. 30% of them had already other pregnancies (children or abortions). 46% of them had access at contraceptive information but did not use them. The rest used contraceptive methods but inconstant. The reasons for not using them anymore were: forgetting, fearing of side effects, partner’s resistance (for not using condoms). In spite of the large access to contraceptive methods and efforts of education in sexual and reproductive health for most teenage girls there is a continuous trend towards increasing the rate of voluntary abortion in that category.

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Confirmation of the anencephaly diagnosis: perception of the women on the interruption of the gestation

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In Brazil abortion is a crime and selective abortion of non-viable fetuses is prohibited. Health services, to avoid criminal liability will not terminate pregnancies, without prior judicial approval. This research has the objective to analyze woman's reasons for maintenance or interruption of gestation and their perception on the necessity of request of judicial authorization when they decide for the interruption. This is a qualitative study, where half-structuralized interviews were carried through with twelve gravidas from July 2008 to February 2009. All diagnosis of anencephaly was confirmed in the Fetal Medicine Service of the Fernandes Figueira Institute in Rio de Janeiro. With the use of content analysis technique the preliminary Results of the analyze data disclosed that the factors that most influenced the women who had decided for the maintenance of the gestation was the most delayed time when the diagnosis of anencephaly was made during pregnancy, the question of the religious faith and the hope of that some miracle could happen until the time of the birth. For the women who decided for the interruption of pregnancy the factors that influenced in favour of this decision were the precocious diagnosis of anencephaly, the support of family and friends, as well as the perception that interruption would shorten an inevitable suffering. For all interviewed gravidas the necessity of judicial authorization for the interruption of pregnancy would have to be abolished and the decision be taken only between the medical team, the women and her family.

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An ethical orientation for neonatal intensive care of preterm infants at the edge of viability

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Introduction: In borderline situations in medicine and especially in neonatology different moral concepts and values collide, and parents and clinical-staff have to establish a common basis for communication. In emergency situations we often decide with incomplete knowledge and discuss with context-open terms. Language is device and obstacle, and it takes a more critically reconsidered and less “personative” language use in this setting.

Material & methods: The study population (n=141) covers four samples of clinical-staff (n1=72) and parents of preterm and in-term infants (n2=69). The survey contains mixed standardized questionnaires and half-standardized interviews. The data analysis is carried out graphically and statistically describing, discussing the Results in language-ethics analysis.

Results & Summary: The study is work in progress. The Results should help us using context-open terms sensitively and phrasing linguistically distinctly and empathically. For example, participants were asked about the most important ethical principle in medicine – 62.3% of parents and only 12.5% of clinical staff chose “fairness”, whereas “autonomy” was majorly important for clinicians with 40.3%. Additionally, the contents of these value terms vary considerably as well.

In the care of preterm infants we have to handle each case individually and make context-sensitive decisions, geared to the consequences for all involved. This study tries to give an orientation in (im-) possible decision-making using “values clarification”. We aim to identify the differences between the “realities of communication” of parents and clinical-staff, who should take the responsibility personally and answer impartially to each child’s “vis vitalis”.

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Ethical concepts in education at perinatal medicine

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Ethics rooted on philosophy and mainly moral aspects, considering the answers of the questions; "what is right-good" and "what I or we ought to do". This aspect will be also considered for the education. The conception based on the international statements, especially on the “Child Rights, Articles 28 and 29”. Professional ethical precepts are summarized as: 1) Specialize, 2) Responsibility, 3) Trust, 4) Equity, 5) Organize, 6) Fully approved by legal and law regulations, 7) The knowledge and application techniques are for the contemporary situations with continuous developmental evidence based medical science, 8) Efficiency, effectiveness and acceptable, 9) Rights, 10) Continuous evaluation and reasoning, 11) All other ethical conducts must be completely and obligatorily performed. Educational grading will be arrange for the students, interactive way, because theatrical educational method; drama, has the highest remembrance ratio. General Considerations: 1st STEP: To become a partner. 2nd STEP: Application of the knowledge. 3rd STEP: Detailed approach. 4th STEP: Evaluation (routine, secondary and intensive care). 5th STEP: Teaching & Training (Proficiency education). 6th STEP: Academic education.

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Maternal hypoxic brain injury at the end of 1st Trimester

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Heart attacks and other cardiovascular diseases are among the most common medical emergencies in Germany. Mainly men and women of higher age are affected by these diseases. Rarely women in reproductive age are concerned. We report a case of a 41-year-old woman in the 13th week of pregnancy suffering from an extensive myocardial infarction, followed by cardiac arrest and survival after resuscitation. In a persistent vegetative state the patient got intense medical care and pregnancy was continued over a period of 22 weeks until the 35th week of pregnancy. Due to premature rupture of membranes in the 34+2 weeks of pregnancy a caesarean section was performed with development of a healthy boy. Despite premature birth he developed in time and without any delay. No neurological deficits were detected. Postpartum it was confirmed that the antenatal incurred neurological damage of the patient was irreversible. Postpartal the mother was transferred in a nursing home for further care near home.

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Discrepancies between the need for and the provision of information prior to the administration of centrally active medication during labor

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Objectives: Reducing the gap between current practice and women’s needs by determining what and how much information women are given before they receive centrally active medication during labor. Comparing the provided information against the information women want to receive. Assessing the degree to which women recall provided information. A critical discussion of the ethical questions arising from the findings.

Materials and Methods: Covered non-participant observations of labors, focusing on the content and amount of information provided by midwives either freely, or upon request of the laboring woman. Postnatal semi-structured interviews to assess women’s preferences as well as their recollection of given information.

Results: Less than 50% of the women were informed about the pain relieving properties of the medication. Only 85% were aware of why they had received the injection at all. 46% of the women wanted information about possible physical effects on themselves and 33% would have liked information about possible psychological effects. 69% of the women wanted to know about possible effects on their infant. 31% of the items judged as important by the women were provided by carers, and 15% of these were subsequently recalled. Recollection of items judged as unimportant was similar.

Conclusions: Information about centrally active medication administered during labor tends to be limited and rather indifferent and vague. The discovered patterns suggest that there is potential to improve the provision of information during labor.

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Effect of DRG introduction on distribution of admission weights in very low birth weight infants

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Background: Admission weight to Neonatal Intensive Care Units is used in several DRG systems to assess reimbursement by health insurances for premature infants. We aimed to investigate whether the introduction of the German DRG system in 2004 had any influence on the distribution of admission weights of premature infants.

Methods: Data of 11,817 infants during two time intervals, 1999-2001 (prior to the introduction of the DRG system) and 2004-2006 (following the introduction of the DRG system), were analyzed.

Findings: There were significantly more infants with admission weights below 1000g (p=0.007) and 1500g (p=0.0019) during the second time period, whereas fewer infants had documented weights above these cutoff borders.

Interpretation: The introduction of the DRG system in Germany has affected the distribution of admission weights of premature infants. Potential reasons for this effect including upcoding are discussed.

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Identification of the problems and Anxiety levels of the women who had elective or therapeutic abortion

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This study is descriptively carried out with the aim of identifying the problems and anxiety levels of the women who had elective or therapeutic abortion. The sample of the study consists of 200 women who applied to the Women's Hospital. The data is collected by using Questionnaire Form and Beck Anxiety Inventory.

In the study, 79.0% of women who had elective abortion (EA) and 52.0% of women who had therapeutic abortion (TA) stated that they had difficulty during decision-making period for abortion. It has been detected that the major problem in this period was the fear for the procedure (85.3% (TA); 25.3% (EA)). It has been specified that the problems mainly faced after the abortion were the pain (25.5% (EA); 45.3% (TA)) and the sadness due to the loss of the baby.

Beck anxiety average point’s being fewer than 21 is evaluated as mild anxiety. In this study, it has been determined that both women who had elective abortion and those who had therapeutic abortion suffer from mild anxiety. It has been indicated that the pre-abortion anxiety point medians of women having had elective abortion or therapeutic abortion are higher than post-abortion anxiety point medians (p<0.05).

Consequently, women having had abortion have problems such as fear and pain as they are not informed sufficiently for the procedure. Therefore, it is thought that nurses' providing women who would have abortion with information and consultancy service before, during and after the procedure will enable them to cope effectively with this process.

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Methodological levels in prenatal psychology

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It has been possible to acquire in very different methodological ways extensive insight into the relationship between prenatal and perinatal experiences and the course of later development, as well as the possibilities of therapeutic and prophylactic intervention. This great diversity of methods, however, makes communication especially with colleagues in medicine, psychology and psychotherapy who are oriented to academic concepts of science sometimes difficult. Since 2007 five different methodological levels in Prenatal Psychology have been formulated:

1. Quantitative measurement and statistical analysis
2. Qualitative aspects
3. Empathic insight
4. Practical experience of midwives, obstetricians and others
5. Cultural psychological comparison

One-sided restrictions at the methodological level hold dangerous problems and decisively limit the quality of treatment and prevention and the validity of Results. On the other hand it is clear that there are no alternatives to integration and balancing of the methodological levels in theory and practice, especially since the unborn baby is not able to chose or to limit himself to one of the levels. The importance for the practical work in the field of obstetrics will be emphasized.

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The role of depression and Anxiety status in the etiology of Hyperemesis Gravidarum

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Objective: To describe the psychological etiology (depression and anxiety levels) regarding Hyperemesis Gravidarum (HG) in a cohort affected pregnant

Materials- Methods: 62 cases with the complaints of severe nausea and vomiting and hospitalized in our clinic with the diagnosis of HG between December 2007-March 2009 were included in the study group, 62 pregnant women who have been followed in Antenatal Care Unit with the routine pregnancy controls, without any complaints of vomiting and whose pregnancy has been continuing without any problems were included in the control group. To measure the depression and anxiety values Beck Depression Inventory (BDI) and State-Trait Anxiety Inventories (STAI-1 and STAI-2) were applied to all of the cases. The mean values of these tests were compared between the two groups. The cut off value in BDI was determined as 17, as the ones above this value were accepted to have a state of depression; the comparison of categorical data between the two groups was made.

Results: Mean age was 26.72±5.45 years in study group while it was 24.98±5.05 in the control group (p=0.088). There were no statistically significance between study and control groups in terms of gravidity, parity (p>0.05). The mean gestational ages during the performance of the inventories were 9.99±3.36 weeks in the study group, and 10.38±1.81 in the control groups (p=0.460).

In %58.1 of the HG cases depression was diagnosed, the ratio was %17.7 in the control group (p<0.001). The mean BDI value of the patients with HG was statistically higher than the control group (17.85±6.61 vs. 10.08±6.71, p<0.001).

The mean STAI-1 and STAI-2 values showed no statistical significance between the two groups (42.37±11.02 vs. 39.10±9.67 p=0.079; 43.56±9.71 vs. 45.02±7.00, p=0.347, respectively).

Conclusion: Regarding to the Results of our study, the depression status of the pregnant can play a role in the HG etiology, but the anxiety status in the pregnant has no place in this disorder.

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Depression with obsessive-phobic disorders in pregnancy

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Although postpartum depression is now a well-known phenomenon, what is also becoming increasingly clear is that depression during pregnancy, especially during the second and third trimesters, is common. The Results of meta-analysis published in 2004 indicate prevalences of 7.4%, 12.8%, and 12.0% for the first, second, and third trimesters, respectively. However, healthcare providers apparently do not recognize the disorder in up to 77% of pregnant women who experience depression.

Despite the high prevalence rate and negative consequences associated with depression during pregnancy, there is limited information to guide women and their physicians about treatment options, and many pregnant women have difficulty obtaining pharmacologic treatment.

Treatment with antidepressants during pregnancy is a difficult issue because of the relative lack of information on possible adverse effects. The Results of a prospective study on adverse birth outcomes for women who used antidepressants late in pregnancy suggest that the medications can have adverse effects. Consequently, a nonpharmacologic therapy, i.e. psychotherapy, is a promising alternative.

The perinatal psychology and psychotherapy in our country has begun to develop actively only during the last few years. Centers on maintenance accompaniment of pregnancy and delivery have been founded, but in this case there is still a lack of specialists in rendering qualified psychotherapeutic help to pregnant women. Therefore, the research actuality of these problems is obvious.

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Birth antecipation, experience and intensity

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Birth is an extraordinary phenomenon which is sporadic in the woman's life Colman, 1999. Anticipated during the gestation, in the woman's fantasies, it will be relived throughout the mother's memories Lopes, 2005. When remembered, it refers to a certain context and the memories associated to it reflect the emotional value attributed to the birth experience Colman, 1999. Most of the pregnant women, during the second and third trimester, dreams, idealizes, and fantasizes the birth moment, Beaton & Gupton, 1990; Pacheco, Figueiredo, Costa, 2005. Based on this assumption, we designed our research with objective to evaluate the emotional intensity of the birth experience as an experience anticipated during the pregnancy and as an experience lived after the birth, with the intent to understand the phenomenon of the birth experience dreamed and lived by the woman. The sample consists of 150 participants of the Obstetrician Service and External Consults of the Hospital S. Bernardo. In a first approach of the participants, between 22/34 pregnancy weeks, after their consent, is applied the Pre-Birth Questionnaire (QPP) adapted from the Birth Anticipation Questionnaire, QAP, Costa, Figueiredo, Pacheco & Pais, 2005. In a second approach, during the fourth week after the birth, it will be applied to the same participants the Post-Birth Questionnaire (QP-P) built based on the Positive and Negative Affect Schedule Scale of Watson & Clark, 1994. With this study we aim to, in the domain of midwifery interventions, know the intensity of each component of the dream, before birth, under the emotional and experience point of view, in a way to provide the women/couple a positive and organizing birth experience.

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The work of a family midwife – health promotion from the beginning of pregnancy to the end of the child's first year of life in particular amongst deprived mothers

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The first „Family Midwives were trained in a mother-Child health Project in Bremen in the 1980’s. The aim of the Project was that Midwives should become involved in the reduction of the perinatal mortality rate in particular with women with a high medical and socio-economical risk. Acting on behalf of health promotion and health prevention, is the focus and characteristic of the work of a family midwife on the psychosocial and medical counseling and support of high risk groups. As a result through intense home visits and home care and the interdisciplinary cooperation with other professionals is the aim of the family Midwife the health prevention and health promotion of mothers and babies with special needs.

The actual operational aim of Family midwives is the early detection and assessment of neglect and abuse of newborns up until the end of the first year. An Early Warning System set up by the family Midwife and her colleagues will achieve this goal. Signs of over challenged and helplessness of the mother/Father must be detected at an early stage. Significant conflicts within the partnership and or the family and violence in the family origin must be ruled out as a potential risk for mother and child during pregnancy and in the post-natal period.

This assessment can be acquired through a close cooperation of work with the social services and other professionals such as Gynecologists, pediatricians and others within the supporting network of the health system.

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Paradigm shift in the obstetrics

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The culture-historical development of the obstetrics chanced during the 19th century. The delivery was a natural phenomenon until this time. Midwives attended deliveries mostly without interventions. The development of the medical sciences triggered a descent of the perinatal morbidity and mortality. But it also trigged new risks and pathologies. The main problem of the medicine leadet obstetric is the interference of the sensitive system of relationships between mother, father, child and midwives as a result of medical routines. A further development of the obstetrics to a relationship leaded obstetrics might to improve the savety of the delivery.

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Postpartum depression: prevalence and risk factors

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Aim: This research is carried out as a descriptive study to determine depression after delivery among women and risk factors affecting depression.

Method: Sampling was composed of 330 women and on postpartum day 1, day 2 and at 6th week totally three interviews were carried out. Percentage calculation, importance test of difference between two means, Cochran Q Test, one way variant analysis (ANOVA) were used in statistically evaluation of data.

Results: According to findings, on postpartum day 1 13 points or over in %16.7 of women. Post partum day 2 and 6th week, In 19.4 percentage of women EPDS point was found as 13 and over. It was determined that according to education level, perceiving income level, marriage age and period, number of pregnancy and living child, situation of willing pregnancy, making decision of pregnancy, having familial depression case, having difficulties at baby care, having thoughts about not being able to care baby, communication with partner, difference between mean EPDS points was statistically significant among women joined in the research (p<0.05).

Conclusions: In conclusion this research finding shown that is very important evaluating mother in post partum period; particularly at 2-8 weeks to be performed by midwife/nurses in terms of having risks for depression.

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Effects of glucocorticoid administration on the fetal ECG

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Administration of glucocorticoids to promote maturation of the fetal lung has been described to reduce fetal heart rate variability. Using the standard ultrasound-based CTG to record fetal heart rate does not allow true beat-to-beat evaluation of the fetal heart rate, nor does it allow for evaluation of the fetal CTG. Using the Monica AN 24 maternal-fetal monitor in combination with the Monica DK software allows for the evaluation of the fetal ECG similar to the long-term ECG recording known from cardiology.

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Hepatic vein cardio-venous communication time is longer in late than in early pregnancy

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Background: Venous pulse waves, as obtained by Duplex Ultrasonography, are a reflection of cardiac right atrial function. The time-interval between cardiac electrocardiographic (ECG) signals and venous Doppler waves is the so-called Cardio-Venous Communication Time (CVCT).

Aim: To evaluate Hepatic Vein (HV) CVCT at different stages of gestation.

Methods: Cross-sectional study in 4 groups of 10 women at gestations (1) 10-14 weeks, (2) 18-23 weeks, (3) 28-33 weeks and (4) ≥37 weeks. Three consecutive venous Doppler waves were recorded at the craniocaudal midportion of the liver from each of the three main branches of HV, simultaneously with an ECG. The time-interval between the ECG P-wave and corresponding A-deflection of venous Doppler waves was measured, without or with correction for gestation-induced changing heart rate (PA and PA/RR respectively). For each group, means and SD were calculated and compared statistically using conventional F-tests for linear mixed-effects models (SAS procedure MIXED).

Results: PA and PA/RR were significantly larger at term than in the first trimester [337±74 versus 220±47msec, p=0.0008 and 0.48±0.15 versus 0.29±0.09, p=0.0009 respectively]. When groups at early-, mid- and late gestation were compared, CVCT increased gradually with gestational age.

Conclusion: CVCT is significantly longer in late than in early pregnancy. This indicates that venous return needs more time to respond to cardiac stimuli with advancing gestation. This observation probably relates to maternal cardiovascular adaptation mechanisms. Our study illustrates that CVCT may be a new parameter to study venous hemodynamics during pregnancy.

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Cardio-venous communication time is shorter in pre-eclampsia than in normal third trimester pregnancy

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Background: Venous pulse waves, as obtained by Duplex Ultrasonography, are a reflection of cardiac right atrial function. The time-interval between cardiac electrocardiographic (ECG) signals and venous Doppler waves is the so-called Cardio-Venous Communication Time (CVCT).

Aim: To compare Hepatic Vein (HV) CVCT between normal third trimester pregnancy (NP) and pre-eclampsia (PE).

Methods: Cross-sectional study in 2 groups of 10 women with NP or PE at gestation of 28-33 weeks. Three consecutive venous Doppler waves were recorded at the craniocaudal midportion of the liver from each of the three main branches of HV, simultaneously with an ECG. The time-interval between the ECG P-wave and corresponding A-deflection of venous Doppler waves was measured, without or with correction for PE-induced changing heart rate (PA and PA/RR respectively). For both groups, means and SD were calculated and compared statistically using conventional F-tests for linear mixed-effects models (SAS procedure MIXED).

Results: PA and PA/RR were significantly shorter in PE than in NP [213±68 versus 297±93 msec, p=0.0345; 0.25±0.09 versus 0.42±0.14, p=0.0042 respectively].

Conclusion: CVCT is significantly shorter in PE than in NP. This observation probably Results from PE-related maternal cardiovascular maladaptation. However, interference from antihypertensives or other medication in the PE group can not be excluded. Our study illustrates that CVCT may be a potential new parameter to study venous hemodynamics during pathological pregnancies, in particular PE.

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Safety of Out-Of-Hospital Birth: Results of 42,154 births started at Home or in a birth centre over a 5-year period in Germany

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Study question: What are the outcomes related to safety when mothers plan to have their baby at home or in a birth centre?
Method: We used routine data collected by QUAG (Association for Quality in Out-of-Hospital Births) for a retrospective cohort study of out-of-hospital births, documented by midwives all over Germany, 2000 – 2004. The study population included 42,154 women starting birth at home or in a birth centre (2000 – 2004).

Results: Pregnancy: Half of all pregnant women (45%) did not have any problem in pregnancy. Birth: During birth nearly all mothers (99%) were supported by someone in addition to the midwife. Most primiparae (90%) had experienced a vaginal spontaneous birth. The transfer rate during birth was 12.5% of all births. Birth injuries: 86.6% of all primiparae with vaginal birth had neither severe tears (grade III or IV) nor episiotomies. The overall rate of caesarean section ranged on a relatively low level – for primiparae (9.1% for all births). Outcome of the child: While the prenatal mortality rate was very low (1.61 per 1,000 births) a high rate of children born alive had a 5 minutes Apgar score of equal 8 or above (98.1%). The transfer rate of all children born out-of-hospital was 3%.

Discussion: Results of this study of over 42,000 out-of-hospital births in Germany suggest a good outcome for mother and child.

Conclusion: The international discussion should lead to a common understanding of how to assess safety in out-of-hospital births.

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Morbidity of newborns from adolescent mothers

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Morbidity among newborns from adolescent mothers is on the increase at Clinical Centre of Montenegro.

Methods: We analyzed 156 newborns from adolescent mothers with an age ≤19 years during the period of two years (January 2007 - December 2008). We studied the risk factors, clinical findings and prognosis of every infant.

Results: There were 5959 deliveries, where 156 (2.6%) were adolescent mothers, 76.3% were normal deliveries, 21.4% caesarean, 2.3% vacuum extractor. The maternal age varied between 14.5 and 18.9 years (mean=16.7). The newborns birth weight varied between 1,270g. to 4,060g. (2,665±525g); there were 11.8% preterm, 4.5% hypotrophycus. Perinatal asphyxia occurred in 6.4% of the cases and 1.2% presented congenital malformation. There were pathologes in 39.8% of the cases, mainly obstetric trauma, respiratory distress and jaundice.

Conclusion: The prematurity, birth weight ≤1,500g., perinatal asphyxia, respiratory distress occur more frequently among newborns from adolescent mothers ≤17.

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The effect of fasting on the fetuses during Ramadan

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Objective: To evaluate the effect of fasting on the fetuses during Ramadan

Material-Method: 45 pregnant women who were fasting in Ramadan with uncomplicated pregnancies of ≥28 weeks of gestation (WG) admitted in 2007 and 2008 were included in the study group. The control group consisted of 45 healthy pregnant women at similar WG who were not fasting. In the study group the cases were evaluated after 3 pm to perform at least 12 hours of fasting. Non-stress test (NST), biophysical profile scoring (BPS) and Doppler (umbilical artery (Umb A), middle-cerebral artery (MCA), uterine arteries (UA)) investigations were performed to evaluate the fetal well-being. The results were compared between the groups.

Results: The mean age, the mean gestational weeks during the evaluation were similar between the groups. In all the cases there is variability on the NST. The accelerations and fetal movements on the NST were fewer in the study group (p<0.001, p=0.004 respectively). The ratio of non-reactive NST was 37.5% in the study group while it was 11.1% in the control group (p<0.001). The amniotic index levels were similar between the two groups (p=0.749). The cases who had BPS lower than 7 were 14.8% in the study group while it was 4.8% in the control group but this difference was not statistically significant (p=0.201).

There was no statistically significant difference between the groups in mean flow velocity and resistance in the Umb A, MCA, UA (p>0.05).

Conclusion: Although BPS and Doppler investigations are not affected statistically significant from the fasting, fetal movements decrease and the ratio of non-reactive NST increases significantly. According to these results; fasting during Ramadan may affect the fetuses negatively after 28 WG.

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Orofacial clefts and maternal stress authors

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Background: Cleft lip and cleft palate are the most common birth defects affecting about one in 700 infants a year in USA. A cleft is an opening in the upper lip, the roof of the mouth (plate) or both. Both genetic and environmental factors affect the prevalence of cleft defect.

Methods: We review the Orofacial clefts and maternal stress

Result: The risk factors include: exposure to cigarette, certain viruses, nutrition deficiencies in mother particularly a lake of folate, race, family history, sex, obesity. Studies suggest that maternal psychological stress can increase the risk of congenital malformations, including: NTDs and orofacial clefts. In studies has been observed that at least one stressful event during the preconception period was associated with a prevalence odds ratio of 1.4-1.5 for the delivery of infants with cleft lip and cleft palate and other defects such as studies suggest that maternal psychological stress can increase the risk of congenital malformations NTDs and cardiac defects.

Conclusion: The women who experience stressful life events around the time of conception or early gestation may be at increased risk of delivering infants with certain congenital anomalies such as cleft lip and cleft palate. So psychological consult especially in women who suffer stress is needed for prevention of some disadvantage of stress disorder such as orofacial defects.

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Pregnancy outcome and neonatal health by mothers aged 40 years and over

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Objective: Delayed childbearing is a known risk factor for adverse perinatal outcomes, including abortion, stillbirth, preterm delivery, low birth weight, caesarean section, pregnancy-induced hypertension, and chromosomal defects. Our study analyze the risk factors for worse pregnancy outcomes in women aged 40 and over in a tertiary center not used to perform medical-assisted reproduction.

Materials and methods: We collected data about women who delivered in our Clinic between January and July 2005, excluding multiple pregnancies. Statistical analysis was performed using R (version 2.7.0) and considering statistically significant a p<0.05.

Results: Among 643 selected women, 50 are 40 or older, and 638 younger. Advanced age correlates with higher BMI (p=0.056) and seems to increase the risk of gestational hypertensive disorders (p<0.05) and gestational diabetes (p<0.05), caesarean sections (p<0.05) or operative intervention during vaginal delivery (p=0.089), neonatal clavicula fracture (p<0.05) and stillbirth (p<0.05).

Conclusions: Advanced aged women seem to have higher risk of pregnancy complications, such as gestational hypertension and diabetes, higher risk of neonatal clavicula fracture and stillbirth, and undergo more frequently to caesarean section. Fortunately, the increasing frequency of advanced age pregnancy is accompanied by an improvement in perinatal care, making advanced maternal age every time more compatible with successful pregnancy.

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Organ-specific cardio-venous communication time is gestation-dependent

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Background: Venous pulse waves, as obtained by Duplex Ultrasonography, are a reflection of cardiac right atrial function. The time-interval between cardiac electrocardiographic (ECG) signals and venous Doppler waves is the so-called Cardio-Venous Communication Time (CVCT).

Aim: To compare CVCT between liver (L), right kidney (RK) and left kidney (LK) in pregnant women.

Methods: Cross-sectional study in 4 groups of 10 women at gestations (1) 10-14,(2) 18-23,(3) 28-33 and (4) ≥37 weeks. Three consecutive venous Doppler waves were recorded from each of the three main branches of Hepatic Veins and from the Renal Interlobar Veins of each kidney, simultaneously with an ECG. The time-interval between the ECG P-wave and corresponding A-deflection of venous Doppler waves was measured with correction for gestation-induced changing heart rate (PA/RR). For L, RK and LK means and SD were calculated at each stage of gestation and compared statistically using conventional F-tests for linear mixed-effects models (SAS procedure MIXED).

Results: In the first trimester PA/RR was significantly shorter in L than in RK and LK [0.29±0.09 versus 0.36±0.09, p=0.0137 and versus 0.38±0.12, p=0.0129 respectively]. Interkidney differences were not significant. Similar results were found for the second trimester, but were not observed in the third trimester or near term.

Conclusion: In early gestation, CVCT is shorter in liver than in both kidneys, which relates to the anatomical distance to the heart. This characteristic of normal physiology is gestation-dependent: probably due to maternal cardiovascular adaptation mechanisms, it is not observed anymore at term.

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Macrosomic newborns from nondiabetic mothers

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Aim: of this study was to point out prenatal activation of the immune system in macrosomic newborns with neurological dysfunction.

Methods: This study include 30 term macrosomic newborns (PTM>4000g) from nondiabetic mothers. Mother’s case history, neurological assessment, laboratory examination (blood cell count, NBT test, serum immunoglobulin levels, lactate dehydrogenase and creatin phosphokinase activities, glycemia, ultrasound examination of CNS, have been analyzed.

Results: All mothers had pregnancies complicated with multiple and diverse acute and chronic disorders. The most frequent problem were recurrent urogenital infections, no one had gestational diabetes. Neurological dysfunction was present in 86.6% newborns (hypotonia, hypertonia, altered reflex activity, convulsions). Ultrasound examination of CNS showed intracranial hemorrhage in 43.3% and cysts in plexuses chorioidei in 26.6%. Moderate parental asphyxia was present in only 16.6%. Laboratory findings showed: elevated level of total serum IgM, increased absolute number of neutrophyls, monocytes and NBT positive cells, increased activity of CPK and LDH, transient hypoglycemia in 83.3% of newborns.

Conclusions: Increased serum IgM, increased absolute number of neutrophyls, monocytes and NBT positive peripheral blood phagocytes, indicate prenatal activation of immune system and inflammatory cascade. Inflammatory cytokines may cause neuronal and white matter damages during development of CNS. IL- 1 beta, the main mediator of early inflammatory response in CNS, can induce increased production of IGF-1 in all fetal tissues, Resulting in fetal macrosomia, even in absence of maternal hyperglycemia and fetal hyperinsulinism. These disturbances can be common etiopathogenetic factor of fetal overgrowth and neurological dysfunction.

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Relation of cord blood Vitamin D levels with Regulatory T cells in healthy newborn infants

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Vitamin D plays a central role in calcium and phosphate homeostasis and its essential for the proper development and maintenance of bone. Recent studies show that vitamin D is effective for different tissue functions in addition to bone metabolism. Vitamin D has immunomodulatory capacities in vivo and in vitro. Regulatory T cells (Treg) regulate effector T cell functions in order to prevent the autoimmune reactions that can occur because of immune tolerance impairment. In newborn and infancy, the important role of Tregs on the allergic disease such as atopic dermatitis and cow’s milk allergy was demonstrated. They have also role to control inflammatory reactions against microorganisms. Vitamin D induce dendritic cells (DC) in order to function treg’s modulation of immune tolerance (in allergy, inflammatory response and autoimmunity). In this study we aimed to study association of cord blood vitamin D levels and the regulatory T cells. The study group comprised of 101 newborn whose gestational age was 38 weeks or more. Cord 25(OH) D levels was measured and CD4, CD25 was analyzed. Newborns were divided into two groups according to the 25(OH) D levels (<12ng/ml and >12ng/ml). There were no difference in white blood cell, total lymphocyte count, T helper, Treg cell percentage and number between two groups. There were also no correlations between vitamin D levels and T cell subset number and percentages.

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Placentar chorioangioma, non-immunologic hydrops fetalis, 'mirror' syndrome and post partum cardiomyopathy - a case report

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We present a case of large, hemodynamically active placentar chorioangioma with unfavorable outcome for the fetus and almost for the mother as well. A 26-year old primigravida presented at 20+5 weeks of gestation with hydramnios and singular umbilical artery. On ultrasound hydrops fetalis with edema, hepato- and cardiomegaly as well as two chorioangiomas of 8x6.5x6 and 5x4x3cm were diagnosed. Therapeutic amniocentesis was performed. Fluid analysis revealed normal findings. Second amnio drainage became necessary; the hydrops progressed with pleural effusions; therefore we discussed the bad prognosis. As ultima ratio fetoscopic LASER-ablation of tumor vessels was offered. At 22+5 weeks, the vessels were successfully coagulated; the masses started shrinking. The hydrops did not improve. On the contrary, the patient was admitted in week 24 with contractions, edema and increased liver enzymes. True preeclampsia did not develop. As she went into labor, we awaited the natural course. At 24+2 weeks a hydropic male fetus was born dead. Placenta histology confirmed the diagnosis. Immediately post partum a drop of oxygen saturation with signs of left heart failure occurred. The patient was transferred to the ICU and treated for the suspected diagnosis of post partum cardiomyopathy: after three days of intensive care and bromocriptine rapid improvement was observed; two weeks later she could be discharged.

Our patient showed the complete set of complications possibly associated with placental chorioangioma. We interpret the preeclampsia-like symptoms as 'mirror'-syndrome with NIHF. The coincidence with post partum cardiomyopathy to our knowledge has not yet been described.

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Ballantyne syndrome of fetal cardiac origin

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The feto-maternal unit is exposed to multiple and reciprocal interactions. Usually this concerns materno-fetally directed events.
In contrast severe fetal hydrops of different origin e.g. caused by Rhesus isoimmunization and infectious agents may lead to a maternal symptom complex first described by Ballantyne as a mirror syndrome. Pre-eclampsia-like excessive edema related maternal weight gain with moderate urine albumine excretion is not always accompanied by significant blood pressure rise.
We present a case of a 26 year old primigravida first seen in the 21st week of gestation with generalized fetal hydrops, moderate fetal ascites and fetal pericardial effusions. Fetal echocardiography showed an Ebstein anomaly. Other fetal defects could be excluded as well chromosomal alterations. Extensive work-up gave negative Results for immunological and non-immunological origins of fetal hydrops.
The patient was offered termination of pregnancy because of poor fetal prognosis. For ethical reasons the family refused this option.
She presented three weeks later with massive maternal weight gain, extreme edema and hypertension. Pleural effusions were moderate upon admission.
Pregnancy was terminated because of deteriorating maternal condition.
In the immediate postpartum period she developed extreme bilateral pleural effusions, excessive hypertensive blood pressure and a progressive nephrotic syndrome.
In conclusion fetal cardiac defects such as Ebstein may not only lead to fetal hydrops but also to severe clinical maternal consequences. Thus a Ballantyne syndrome must be included in counseling patients with this fetal condition to avoid detrimental maternal outcome.

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Maternal Hyponatremia and HELLP syndrome

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Maternal hyponatremia with HELLP syndrome is very rare and very few cases reported in literature. We present a rare case of maternal hyponatremia and HELLP syndrome. She presented in labor at 39+3 weeks gestation with uneventful pregnancy so far. She had prolonged a latent phase and had a normal delivery. She felt dizzy and had a fall 3 hours post delivery. She was unconscious for 45 minutes. Blood tests revealed hyponatremia, elevated liver enzymes and low platelets. She had more than 2 liters fluid intake during labor.

The most likely cause could be elevated levels of vasopressin secondary to severe maternal hypovolemia and increased fluid intake. A recent study has found moderate hyponatraemia in 26% of the women with a total fluid intake of more than 2.5 liters. It is very important not to rapidly correct it. The recommended rate of correction is 2mmol/L/hr. The patient recovered well.

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Postpartum depressive disorder and early attachment. A follow up evaluation of standardized videotaped mother-child interaction

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Introduction: Postpartum depression (PPD) is a frequent mental disorder but it often goes undetected and therefore is not treated sufficiently. PPD poses a high risk of malfunction of mother-child attachment, particularly with regard to the mother’s emotional availability. PPD is already known to influence the cognitive, emotional and mental development of the infant. Therefore, mother-child interaction is of central importance for counseling and therapy of depressive mothers and their infants.

Method: After the screening of over 700 women for an 18 week postpartum period by Edinburgh Postnatal Depression Scale (EPDS), nine women reached classification for depressive disorder according to DSM-IV/ICD-10 criteria confirmed by the Structured Clinical Interview for DSM IV (SKID-I). They were matched to nine mentally healthy mother-child dyads (SKID-I). The quality of mother-child interaction was compared for both groups at the age of 18-22 weeks of the infant. Video-tasks were accessed using the "still-face-paradigm" and rated with the Coding Interactive Behavior Scales (CIB).

Results: Depressive mothers showed significantly reduced interaction quality compared to the healthy control group. Demonstrating and explaining these findings to mothers was well accepted and encouraged their motivation for therapy.

Discussion: Screening mothers for postpartum depression and offering videotaped analysis of mother-child-interaction in postpartum depression is recommended. In combination with individual counseling this is an important contribution to primary and secondary prevention and therapy of mental disorders, both in mothers as well as in infants.

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Sideways in treatment of obese child: a personal experience

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The prevalence of overweight children and adolescents is one of the most important public health challenges today. The impact of this early obesity extends into adulthood: increased mortality and morbidity from a variety of conditions and adverse socio-economic consequences. No single approach to the treatment of childhood overweight has been demonstrated to be more effective than another. Challenges faced in managing obese child is selecting the approach that will be adhered to on a long-term basis, involving whole family in the health lifestyle regarding the child’s age, sex, cultural and entire environmental background.

Aim: finding the best therapeutic approach for obese child.

Methods: a two years follow up effects of lifestyle modification (dietary, physical activity, psychotherapy) and/or drug (sibutramine) for treating obesity in 40 children (mean age 13 years) with the support of family members. Children with eating disorders, diabetes mellitus, secondary or syndromic obesity were excluded. Lifestyle interventions, focused on physical activity and changing eating habits, with behaviorally orientated treatment were implemented in all. Sibutramine used in children with BMI ≥95th percentile (20 children). Reduction in overweight at 6, 12, 18 and 24 months follow up was observed in all children; addition of sibutramine showed more significant weight lost in longer time period (15% vs. 8% after two years) with less psychological disturbances and better self-oriented outcomes.

Conclusions: combined behavioral lifestyle interventions have a significant and meaningful reduction in overweight in children and adolescents. Pharmacotherapy is an effective adjunct to lifestyle interventions in morbid obese child.

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Severe Intrauterine Growth Restriction (IUGR) – Growth and development evaluation

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Background: Newborns with IUGR had suffered one anoxia that disturbed their growth. Cognitive impairment, motor delay, language and behavior problems can occur.

Aims: Growth and development evaluation of prenatal diagnosed severe IUGR.


3/13 parents showed concerns on PEDS.

Commentaries: Currently, average age 31 months, 4/13 with persistent weight <P5. Development impairment reported on 3 areas: language, gross and fine motor. The parents who have affected children are worried about that development delay, according PEDS.

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Neuromotor and cognitive development in preterm infants with normal brain maturation evaluated by serial diffusion tensor imaging (DTI)

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Many neurological and neurobehavioral disorders begins in early structural and functional cerebral organization and maturation. DTI is a powerful technique to explore the structural basis of normal brain development and provides early evidence of hypoxic-ischaemic damages. Aim of the study is to estimate the neuro-cognitive development of children with any brain damage at conventional MRI and to correlate maturative modifications of the brain and the acquisition of the normal competences.

From 2005 to 2006 12 infants, in-born at GA 31.6 wks (1460g±320) with normal MRI were enrolled and studied with at least two examinations with conventional study and study of DTI (1st examination at GA <34th wks, 2nd at 40wks post-conceptional age, 3rd at 2nd month of corrected age). Griffiths’ scale was performed at 20 months CA. Calculation of quantitative parameters of Dm and FA studied in vivo the brain maturation, showing normal maturation trend in all children and in all regions of interest calculated, (reduction Dm, increase FA). Areas with precocious myelination (commissural and deep projection tracts) were distinguished from those with slower and late maturation (association and subcortical projection tracts) and also normal values were identified for revaluations. Otherwise in absence of predictive clinical and neuroradiological datas, the development of the neuromotor and cognitive competences underlined disabilities stronger in the area of the performance and less evident in the area of the visual-motor coordination. In preterm with normal MRI and normal maturation trend Griffiths scales are important instruments for screening neurocognitive delays.

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Follow-up of children who had suffered from intrauterine hypoxia of various degree and duration in their first year of life

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Aim of study: to assess health status of children who had suffered from intrauterine hypoxia of various degree and duration according to antenatal cardiocography Results.

Material and methods: the study included 50 women and their 50 children. All babies were delivered at term by caesarean section because of antenatal CTG signs of progressive fetal distress. Newborns were examined in neonatal period and at month 3, 6 and 12. We performed general clinical examination and used additional methods for health status evaluation (including The Clinical Adaptive Test/Clinical Linguistic and Auditory Milestone Scale - CAT/CLAMS).

Results: The most difficult postnatal adaptation was observed in children in whom ill-defined antenatal CTG signs of fetal distress had persisted for approximately 3 weeks. The fact that these signs are ill-defined wrongly assures an obstetrician that there is still a possibility to prolong pregnancy under close fetal surveillance. However, physical development in this cohort of children in their first year life is characterized by severe disadaptation, slow weight gain and more profound harmonical disturbances.

Conclusions: Although antenatal CTG remains the most accepted method for fetal condition monitoring, there is no consensus on how long conservative management in patients with signs of fetal distress should be continued and when exactly these babies should be delivered. Introduction of new diagnostic tools might help to improve obstetrician's approach.

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Our experience, estimation of the vitality of the newborns born with vaginal childbirth with no pain

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Today epidural analgesy is the most often used method for no pain in vaginal childbirth. In some hospitals in the world the percent of applicable epidural is about 50% and in some others even more.

-Through vital parameters (Apgar score and ABS) to show vitality of newborn, childbirth with epidural analgesy in comparison with newborn without pain in vaginal childbirth.

–263 vaginal childbirth are processed and from them 181 were with epidural analgesy, 82 with without it. All children as parameters for vitality are used Apgar score in first and in fifth minute and ABS and it is made comparation between both analyzed groups.

–In group of 181 childbirth with epidural analgesy, there are not any babies with Apgar score in first minute between 0-6 points, with 7 points were 3 babies and other were with 8 or more points in first minute. From 81 childbirths without analgesy there are not any babies with Apgar score in first minute between 0-6, with 7 points were 4 babies, and others were with 8 or more points. Apgar score in fifth minute in both groups was over 8 points. In relative of the way of completing the childbirth in realitv of use of vacuum extraction in second birth time in 263 childbirths was 5, and 2 were with epidural analgesy, and other 3 without analgesy.

- Epidural analgesy doesn't make bigger the risk of finishing the childbirth using vacuum. There is no difference in grades for vitality on childbirth in both groups, but the satisfaction of pregnant woman with epidural is bigger.

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Follow up study of psychomotor development in neonates with Rhesus isoimmunisation

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Introduction: Rhesus isoimmunisation in neonates should be promptly treated to avoid toxic effects of high bilirubin level on brain cells known as Kernicterus. Nowadays, it is a very rare complication due to modern treatment (EST, Phototherapy). Yet we can clinically recognize (neurologic assessment) neonates with high levels of bilirubin in first days of life although there is little evidence showing adverse neurologic outcome in infancy.

Aim: is to notice if there is any significant differences in neurologic outcome during the first year of life in children with neonatal haemolytic disease treated with or without EST.

Material and Methods: Prospective clinical study in 100 term neonates with Rhesus isoimmunisation during 5 years period who formed 2 groups a) with EST and b) without EST. Neurological assessment is done at 6 weeks, 3, 6, 9 and 12 months. Psycho test at age of 9 and 12 months.

Results: Hypotonia in 50%. Hypertonia in 2% without differences between groups. Psycho test reveals normal score in both groups but at the bottom range (RQ 91.66) with significant difference between boys and girls (90.16:93.16).

Conclusions: There is no evidence of pathologic psychomotor development. Psychomotor development was in the range of the lowest normal level for age. Slight differences in psychomotor development were recognized in infants of different sex. There is a possibility that CNS in male neonates is more sensitive toward toxic effect of bilirubin.

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Prospective clinical study of Amikacyn level in neonates with severe infection

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Introduction: One of the main problems in neonatal practice is to choose antibiotics that can efficiently solve severe neonatal infection without leaving consequences to immature renal function.

Aim: of our prospective study is to 1) measure blood level of Amikacyn in neonates treated with Amikacyn during 2 weeks 2) to compare our Results to nontoxic concentration of (20 umg/l) 3) to find out if there are any differences in Amikacyn level between neonates in early and late neonatal periods as renal function develops in first days.

Material and Methods It is prospective clinical study of 60 term neonates hospitalized on our neonatal department, treated with Amikcyn in therapeutic doses (12-15mg /kg BW/24h) during 14 days divided in:

Experimental group <7 days of life
Control group >8 days of life. Their blood sample for Amikacyn concentration is taken in these points 1) 10 minutes after the first application of Amikacyn 2) a few minutes before the second application,3) before the last application,4) 10 minutes after the last application and 5) 24 hours after last applications.

Results and Conclusion: Amikacyn blood levels in our study are beyound nontoxic dosis according to literature data.

There is no significant differences between Amikacyn levels in all points of measurement in experimental and control group. It is safe to treat neonates even in the first week of age with Amikacyn although renal function is starting to developing after birth.

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Uterine myomas in pregnancy: Preliminary data of an ongoing study

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Introduction: Uterine myomas are the most common bening tumors in women of reproductive age which also make it common in pregnancy and affect the pregnancy outcome. We presented obstetric outcomes of myoma uteri detected during pregnancy.

Patients and Methods: 33 pregnant women with diagnosis of uterine myoma between April 2008-February 2009 were included prospectively to determine the obstetric outcome.

Results: The mean age of the patients was 33. Seventeen of them were primigravid. The mean size of the myoma was 58.6mm. In 18 patients, myomas were detected at the anterior uterine wall while 15 were at the posterior. 13 patients had multiple myomas. 10 of the patients had severe pelvic pain mostly during early second trimester which lasted about 5 days. 7 of these had myomas on posterior uterine wall with a mean size of 75mm. 4 patients suffered bleeding in early pregnancy and another 4 had spontaneous miscarriages. The mean gestational week at delivery was 39.1. Of the 29 term pregnancies, 26 (90%) delivered by caesarean section and 3 (10%) per vaginum. Malpresentation rate was 34% (10 out of 29). Myomectomy was performed during caesarean section in 4 patients. 3 of them needed blood transfusion. The mean birth weight was 3,100 gram. One pregnancy was complicated by SGA. No preterm delivery was seen.

Discussion: Depending on the size, location and associated factors, myomas can cause complications. In our study posterior uterine myomas were more frequently complicated by pelvic pain. A successful pregnancy and delivery is common with appropriate surveillance and supportive management.

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Postpartum curettage and the prediction of retained products of conception

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Aim: To assess whether delivery details, clinical features at presentation, echographic image before curettage could accurately predict the presence of retained products of conception (RPOC) following a postpartum curettage (PPC).

Methods: A retrospective chart review of patients who underwent a PPC at a tertiary referral hospital over a 2-year period. We included only gestations with more than 37 weeks. All cases with retained placenta were excluded.

Results: Forty nine patients were included in the study and thirty (61%) patients who had histological evaluation demonstrated retained product of conception. Most (60%) postpartum curettage was done within 48 hours post partum. The clinical features at presentation were unrelated with final histology. However, patients with more than one birth were found more likely to have RPOC (p<0.05). The sensitivity and specificity of ultrasound in detecting RPOC was 80% and 60% for a presence of a thickened endometrium of more than 21mm. Analyzing the type of RPOC we had more membranes in a younger women without symptoms, with only one birth, and having PPC earlier.

Conclusion: A PPC has a low diagnostic yield. Ultrasound has a low specificity (60%) in detecting RPOC. While the therapeutic benefit of PPC is unclear, expectant management should be evaluated especially in the presence of young women without symptoms, with only one birth, and a ultrassound with thickened endometrium of less than 22mm.

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Outcome of antenatally suspected congenital sequestration malformation of the lungs in Wales: 7 years experience 2000–2006

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Objective: To determine outcome of antenatally suspected congenital sequestration malformation of the lungs over a 7 year period in Wales.

Methods: A retrospective study of babies with antenatally suspected sequestration. Data was obtained from the CARIS (Congenital Anomaly Register and Information Service for Wales), Neonatal and Radiology databases and Surgical and Respiratory records.

Results: 28 cases of sequestration were suspected antenatally. There was no hydrops and none of the conceptus required ante-natal intervention. There was no pregnancy loss. In 6(21%) of cases the lesion became less visible in subsequent ante-natal scans.

Postnatal information was unavailable in 4 cases. Post natal CT scan of the chest was performed in 21(75%) of cases of which 16 (76%) showed sequestration of lungs and 5(24%) showed variable lung pathology. Five infants required surgical removal of the lesion between 1 to 5 years. The histology was heterogeneous. Thirty five percent of cases were discharged from the follow up. Fifty percent of cases were still being followed up. Of the 6(21%) of cases with suspected antenatal resolution, 4 did not have post-natal CT of the chest and in the remaining two cases the CT chest findings were heterogeneous.

Conclusion: The majority cases of sequestration are isolated and asymptomatic at birth. Although some appear to resolve antenatally, most persist and post-natal CT scan findings are heterogeneous. Therefore it is recommended that all cases have post-natal investigation and follow-up.

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Long-term outcome of neonatal abdominal wall defects

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Aim: Assessment of long-term Results of the surgical treatment of omphalocoele and gastroschisis in neonatal period and neurodevelopmental follow-up.

Material and methods. Within 10 years (1996-2005) 27 (15 male, 12 female) newborns with mean birth weight 2709g and mean GA 37.5 weeks, were born with congenital defect of abdominal wall (16 with gastroschisis and 11 with omphalocoele). They were treated in the University Hospital in Zabrze. 24 neonates were operated in 1st and 3 in 2nd day of life, 23 newborns had one-step surgery, 4 – multistep surgery using Shuster's method. Ten neonates died in first month of life because of operation complications and other congenital defects. (mainly heart defects) Mean time of hospitalization was 40 days. 15 of 17 survived children in age from 1.5 to 10 years of life were followed-up, included psychophysical development, necessity of post hospitalization treatment and cosmetic effects of operation.

Results. Successive operations were necessary in 5 children with inguinal hernia, 7 children with hernia in cicatrices, one with gastroaesophageal reflux. Cosmetic effect of wall defects operation was good in 8, satisfactory in 4 and bad in 3 children. No neurodevelopmental, sensorial and physical disorders in all 15 children were found.

Conclusion. Congenital abdominal wall defects are serious clinical problem with high mortality in neonatal period. Isolated defects can influence on cosmetic effect with often necessity of secondary correction, but without affecting the normal development.

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Sandhoff disease in infancy-diagnostic

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Introduction: The most common and severe form of Sandhoff disease begins in infancy. It is caused by a deficiency of the enzyme beta-hexosaminidase, which results in the accumulation of certain lipids in the brain and other organs of the body. β-hexosaminidase A (β-N-acetyl-d-hexosaminidase) is a lysosomal hydrolase composed of an α- and a β-subunit. It is responsible for the degradation of GM2 ganglioside

Methods: Symptoms of Sandhoff disease can appear in childhood, adolescence and in adulthood. There was a marked cerebellar atrophy on MRI, and proliferation of abundant PAS-positive foamy macrophages in the rectal mucosa. Ultrastructural studies revealed numerous inclusions in the cytoplasm of retinal ganglion cells and other neuronal cells.

Results: Substrate-specific effects of this mutation were demonstrated by the urinary oligosaccharide pattern. Infants with this disorder typically appear normal until the age of 3 to 6 months, when development slows and muscles used for movement weaken.

Discussion: It is clinically indistinguishable from Tay-Sachs disease, but affects two hexosaminidase enzymes. Differential accumulation of alpha- and beta-synucleins in human lipidoses may be related to functional differences between these two proteins.

Conclusion: Sandhoff disease does not have any standard specific treatment or cure. Signs and symptoms can begin in childhood, adolescence, or adulthood and are usually milder than those seen with the infantile form of Sandhoff disease. ELISA system involving anti-GM2 monoclonal antibodies for measuring GM2 storage in fibroblasts from Tay-Sachs and Sandhoff disease patients are very useful.

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Meckel's diverticulum causing obstruction in neonate

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We report a male newborn of 18 day old presented with a 24 h history of poor feeding and intermittent nonbilious vomiting. His stools were normal.

Case Report: He was born at term and weighed 4.1kg was quite well at birth and passes meconium normally. He was breast-feeding every 3 hours.

On physical examination, the baby appears pale. He has a heart rate of 147 beats/min, respiratory rate 52 breaths/min, blood pressure of 89/52mmHg. and temperature of 36.3ºC.

His cardiac and pulmonary examinations were normal.
The abdomen was soft and mildly distended, without masses.
The neurologic examination was normal for age. His rectal examination was normal.

Diagnostic Studies: The complete blood count, chemical, urine values and blood culture were normal. Stool was negative for virus or bacteria.

Initial abdominal Rx: showed moderate dilated gas filled loops of small bowel, with air in the distal large bowel and no free air in the abdominal cavity.

On the following day, he developed fecal vomiting and X ray findings were suggestive of a small bowel obstruction requiring surgical exploration.

In the operating room, he was found to have a distal small bowel obstruction related to a Meckel diverticulum and ectopic teste.

Treatment was the resection of the entire ileal dilated segment (12cms) with a normal end-to-end bowel anastomosis.

Histopathological examination of the specimen showed dilated terminal ileum and no heterotopic tissue.

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Hyperreactio luteinalis in an uncomplicated pregnancy - A case report

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Hyperreactio luteinalis is a condition associated with bilateral or unilateral enlargement of the ovaries with theca lutein cysts. This pathological entity has been reported to be associated with multiple pregnancies, molar pregnancies, hyperandrogenic state and virilisation, fetal hydrops. There are only a few cases of asymptomatic theca lutein cysts.

We report a case of a 22-year-old primigravida who had a normal booking and anomaly scan. A scan was done at 37 weeks to confirm breech presentation. Both ovaries were enlarged with multiple cysts of size 10 cm. She was completely asymptomatic. A caesarean section was performed at 39 weeks after an unsuccessful external cephalic version. During the operation both the ovaries were enlarged as described in the scan, with multiple fluid-filled cysts. Biopsy of the ovarian tissue confirmed hyperreactio luteinalis. An ultrasound scan performed postnatal at 6 weeks demonstrated complete regression of the cysts with normal ovaries.

This case highlights the fact that theca lutein cysts can occur even in a normal pregnancy and the patient can be completely asymptomatic. If a scan had not been done for evaluation of the malpresentation the cyst would not have been detected antenatally. It also stresses the importance of examination of the adnexa at the time of any caesarean section. If the clinicians are familiar with the appearance of the cyst and the nature of spontaneous regression unnecessary interventions like oophorectomy can be avoided. It also stresses the importance of follow up scans to ensure complete resolution.

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Achondroplasia: Case Report

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Background
Achondroplasia is the most common condition associated with disproportionate short stature, with variable incidence (1/15000-1/40000 births). It is transmitted as an autosomal dominant trait, resulting from a mutation occurring in fibroblast growth factor receptor 3 (FGFR3), 80% are sporadic cases. Prenatal diagnosis is possible after 20 weeks of gestation.

Case Report
A 29-year-old pregnant woman was transferred to this hospital at 20 weeks of gestation because of short long bones had been detected by ultrasonography. Serial ultrasounds performed between 22 and 32 weeks of gestation showed long-bone foreshortening, frontal bossing, macrocephaly and midface hypoplasia. Parents chose not to perform any additional study. The patient was born by caesarean section at 40 weeks and had rhizomelic shortness of limbs, large head, and small chest, characteristic of Achondroplasia. Radiographs showed shortness of the long bones and flaring of the metaphyses. Nowadays, at 12 months, she has sleep roncopathy which is being evaluated and is slightly delayed in her motor development, so she is on physiotherapy and occupational therapy program.

Conclusion
Ultrasound is effective in prenatal diagnosis of achondroplasia allowing not only to counsel the parents about the diagnosis as well as a soon confirmation after birth. In order to improve life-quality of these patients it’s crucial to establish a plan of anticipatory care directed to identify children who are at high risk of complications and intervening to prevent serious sequels.

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Telematics and midwifery postnatal care to the mothers on the sexual and reproductive women’s attention programme in Catalonia, Spain.

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Background: Women and families nowadays seek health information in Internet about maternity care and are able to profit from benefits of e-health and telemedicine form the health services. 
Objectives: To know the effectiveness of telematics intervention to the mothers in the postnatal period in relation to the usual attention related to the women’s opinion, consultation and morbidity on the Community Programme of the Sexual and Reproductive Women’s Attention (PASSIR). 

Methodology: 
Design: Multi-centre study and randomized controlled trial study. 
Setting: Postnatal community clinics of Catalonia, Spain. 
Participants: 400 women which prenatal care has been carried out on the clinics of PASSIR, who are internet consumers. There have been two groups: women of the control group with usual midwifery care and experimental group with telematics intervention with videoconference and phone calls and usual care. 
Method: The intervention has been carried out by the midwives by videoconference and phone to mothers from clinics of PASSIR during the six first weeks of puerperium. Ethics. This project has received the approval of the Ethics Commission. 
Data analysis: A descriptive analysis will be presented as well as bivariante analysis. 
Outcomes: The Results from January to September 2009 will be presented. 
Funding: This research project has been financed by the Institute Carlos III, Minister of Health, Spain. It has also received funds from Health Department of Catalonia.

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Early postpartum discharge in a tertiary center with a wide geographic dispersion

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Objectives: To evaluate the “Early postpartum discharge program” impact in a tertiary hospital characterized by a wide geographic dispersion of its reference population.

Methods and Materials: The “Early postpartum discharge program” was fully developed in our center in 2008. We compared all “Vaginal delivery without complicating diagnoses” (Diagnoses-related group DRG-373) registered during 2008, with a similar historic cohort from 2003. Puerperal readmission were recorded and classified as DRG-376 “Postpartum without operation room (OR) procedures” or DRG-377 “Postpartum with operation room (OR) procedures”. Student-T for independent samples and 2 test, were used for statistical analyzes.

Results: All vaginal deliveries without complications during 2003 and 2008 (2133 and 2304 respectively) were analyzed. No differences were found for any social or demographic characteristics. Mean admission for RGD-373 during 2008 and 2003 was 3.18 days and 2.52 days (p<0.001) respectively, mean difference 0.66 days/patient (CI 95% 0.62-0.69). Overall puerperal readmission (DRG-376 and DRG-377) decreased from 1.98% in 2003 to 1.00% in 2008 (p<0.05), proportions difference 0.88% (CI 95% 0.17-1.56). DRG-376 (without OR) fall from 1.18% to 0.56% (p<0.05), proportions difference 0.62% (CI 95% 0.06-1.17). A non significant drop of readmissions for DRG-377 (from 0.71 to 0.43% (p=0.29)) was observed.

Conclusion: The “Early postpartum discharge program” reduced hospital mean postpartum admission in our centre. This lower mean admission was associated with a significant decrease of the overall rate of puerperal readmissions (DGR-376; DRG-377), particularly without surgical complications (DRG-376).

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Follow-up study of children who were audiologically examined in prenatal and postnatal period

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Early audiological examinations in prenatal period have a great importance as they enable prompt application of early auditory stimulation procedures. The research aim was to examine the auditory perception development in children who were examined by procedure of Prenatal Hearing Screening (PHS) in prenatal period. Research sample comprised 62 children at the age from 3.5 to 4.5 years, who were examined by PHS, and was divided into two groups: children from low risk pregnancies (N1=30) and children from high risk pregnancies (N2=32). The audiological examinations in both groups of children included: transient evoked otoacoustic emissions (TEOAE), tympanometry, pure tone audiometry and comparison of obtained audiological examinations with PHS Results. Results of audiological examinations are discussed in relation to PHS Results and pregnancy conditions.

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**Epidemiologic study of parturients carriers of Hepatitis B and C**

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**Aim:** The recording and the epidemiologic evaluation of pregnant carriers of hepatitis B and C and the comparison of native, gypsy and foreigner parturients who were observed in the Obstetrical - Gynaecological Clinic of Hospital of Pirgos.

**Material-Method:** There was done check and retrospective study in the books of childbirths and in the files of hospitalization of the parturients who we observed at the period 2000 - 2008. We recorded pregnant characteristics like nationality the number of the pregnancy the follow-up at the duration of pregnancy the pregenital check for hepatitis B and C and the paediatrician’s informing for the appropriate treatment of the nursling.

**Results:** In total of 3324 parturients we had 1049 Cesarean sections (31.8%) and 2275 vaginal childbirths (68.2%). The parturients carriers of hepatitis B, 109 (3.3%) presented triple frequency from the parturients carriers of hepatitis C, 37 (1.1%). The carriers of hepatitis B and C are much more frequent in populations of foreigner parturients 1141, 56 (5.1%) and 19 (1.7%) as well as in gipsies 692, 29 (4.2%) and 8 (1.1%) than in the native Greeks 1591, 24 (1.5%) and 10 (0.6%).

**Conclusions:** The progennitical examine of pregnant gives the possibility in the direct immunization of nurslings with immunoglobulin as well as with vaccination for hepatitis B. With advisory intervention and informing on the prevention of sexual diseases the health of female population is improved.

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Drug addict and HCV positive mother and her newborn with multiple congenital anomalies

-Case report-

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Aims: Beside genetic background, congenital anomalies can be also influenced by micro environmental changes as maternal infections. Maternal immune system activation may alter the cytokine network and influence abnormal embryogenesis that leads to congenital anomalies. The aim is to present the immune system activation in newborn with congenital anomalies and activation of the immune system in their mother.

Methods: Red and white blood cell count, hemoglobin and hematocrit level, peripheral blood smear, nitro-blue-tetrasolium test (NBT), serum immunoglobulin level, serum nitric oxide (NO) level, TORCH organisms detected by enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction for Hepatitis C (PCR HCV), clinical and ultrasound examination.

Results: Clinical examination showed multiple anomalies: cheilognatopalatoshisis lat. dex., meningomyeloceela, polydactilio pedis dex., and ultrasound of the heart- AV canalis completa. In the newborn: increased absolute number of NBT positive cells, increased serum immunoglobulin M level, increased serum NO level, PCR HCV DNA negative, were found. Mother is drug addict, HCV positive, treated with IFN-gamma before pregnancy. Their laboratory parameters showed: increased absolute number of neutrophyles and monocytes, increased absolute number of NBT positive phagocytes and increased serum NO.

Conclusions: Altered mother immune system because of chronically infection, during pregnancy, may influence disturbances in fetal growth and development, changes organogenesis and lead to congenital anomalies, because of altered fetal cytokine, growth factors, hormone and neurotransmitters level. The altered laboratory parameters could be an indication of causative and/or Resultant events in children with congenital anomalies.

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Study of hepatitis b in a population of pregnant women.(Polycentric study)

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Aim: To investigate the epidemiology of hepatitis B in the population of pregnant women in Greece.

Material-Method: In total 2,417 women (2,083 Greeks and 334 foreigners) were examined in the 1st trimester of pregnancy. For all of them we measured by the immune-enzyme method the surface antigen (HbsAg), the hepatitis B e antigen (HbeAg), as well as the antibodies anti-HBs, anti-HBc-IgM and anti-Hbe.

Results: a) 42 women (1.74%) were HbsAg positive. 28 of them were Greeks (1.34%) and 14 were foreigners (4.19%), b) 354 women (14.6%) were infected by the virus in the past. These were 271 Greeks (75.2) and 83 foreigners (24.8%). In total, 106 became immune, while 248 didn’t, c) 738 (30.5%) developed anti-HBs antibodies after vaccination, and d) 1283 (53.1%) were negative for all indicators examined. It should be underlined that, therapeutically, gamma-globulin was provided to the newborns of the mothers that were Hepatitis B carriers directly after the labor, as well as the first dose of the Hepatitis B vaccine.

Conclusions: 1) It is, therefore, proved that the Hepatitis B, although rather limited, it still consists a serious health problem in our country. A considerable increase is particularly presented in the foreign population where the percentage of positive HbsAg as well as that of unprotected-unvaccinated women is much higher. 2) Consequently, it is necessary to provide an intensive vaccination program (which will include not only the high-risk groups but the general population) and a systematic informing consultation by all of us.

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Neonatal outcome in pregnancies complicated with preterm premature rupture of membran

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Objective: Preterm premature rupture of membran (PPROM) is the most important cause of preterm labor. PPROM is associated to approximately 3% of all births and 30-40% of preterm birth. Etiology of PPROM is multifactorial and infection is one of the major risk factor. In this study we evaluated neonatal consequences related to PPROM.

Methods: A retrospective study was conducted on 58 preterm neonates from 46 pregnant women with PPROM between January 1, 2005 and December 31, 2008. Maternal evidences and neonatal morbidity and mortality were analyzed.

Results: Out of 1,392 deliveries, 58 (4.1%) were complicated with PPROM. There were 15 neonates with 5 min Apgar scores less than 5. Chorioamnionitis was present in 21 cases; gestational age was less than 28 weeks in 15 of them. Chorioamnionitis and prolonged latency period was higher in the first group with low Apgar scores. Earlier gestational age at the time of PPROM was associated with a longer latency period (<28 weeks: median 28 hours, 28-32 weeks: 8.5 hours, >32 weeks: 8 hours). Earlier gestational age at time of PPROM was not associated with increased early and late neonatal sepsis. Perinatal hypoxia, small for gestational age, patent ductus arteriosis, intraventricular hemorrhage were strongly associated with chorioamnionitis. In spite of a high ratio of oligohydramnios (%81) no pulmonary hypoplasia was diagnosed.

Conclusion: Especially at earlier gestational ages PPROM is still associated with poor neonatal outcome.

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Universal screening strategy for preventing perinatal group B Streptococcal (GBS) disease in Sardinian population

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In order to prevent early-onset perinatal GBS disease, since October 2003 we adopted in our clinical setting the universal screening strategy for GBS detection at 35-37 weeks’ gestation to identify colonized pregnant women to submit to intrapartum antibiotic prophylaxis (IAP). Vaginorectal specimens were cultured in Instant Granada Medium which provides Results in 18-24 hours without requiring high technical ability. It allowed us to perform the test 24 hours a day, 7 days a week. If Results were not available at delivery, risk factors strategy was applied as recommended by CDC on August 2002.

From October 2003 to October 2007 we collected data from 3696 patients out of 5710 who referred for delivery in our Department. GBS colonization in pregnant women was about 12%. In our study population 82% of colonized women underwent IAP. Before October 2003 the prevalence of GBS early-onset disease in our setting was 0.5% of neonates admitted to NICU. In the following years we registered a dramatic reduction of early-onset GBS infections with only three cases of newborns admitted at NICU (0.09%). No increase in infections by opportunistic agents neither maternal allergic complications following antibiotic prophylaxis were detected.

In our experience universal screening strategy proved to be an efficacious and efficient tool in reducing the prevalence of early-onset GBS disease. We believe that it is related not only to identification of women to submit to IAP but also by maintaining health providers alert about the possible onset of GBS disease.

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Distribution of serotypes of group B streptococci (GBS) from newborn and pregnant women in Andalucia

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Objective: To know the GBS serotypes that colonizes pregnant women and cause neonatal disease in our population.

Material and Methods: From May 2007 to October 2008 we have serotyped 14 strains GBS invasive (11 early-onset and 3 late onset) and 150 strains of pregnant women using the Strep-B-Latex slide agglutination test (Statenserum Institut; Denmark) but using a modification of the method (Efstratiou Method). A suspension of GBS from an overnight culture blood agar, was made in 250 µl saline solution. A drop of this suspension was mixed with a 1µl loop of Stratenserum Institut group B latex reagent on a glass slide.

Results: Among isolates from neonatal early onset type Ia (5/11) was the more common, type III (4/11) and type IV (2/11). For the 3 late onset infection the distribution was type Ia (2/3) and type III (1/3). Among pregnant women the type III was more common 50/150, type Ia: 38/150, type V: 21/150, type II: 15/150, type IV: 11/150, non typable: 10/150 and type VII: 3/150.

Conclusion: Compared with previous studies in our population an increase of serotypes IV and V was noted in colonization of women pregnant. “The research leading to these Results has received funding from the European Community’s Seventh Framework Program (FP7/2007-2013) under grant agreement n 200481: Project DEVANI”.

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Neonatal infection and group B streptococcus, what relationship?
Outcomes of the year 2008 in our centre

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Introduction
Group B streptococcus remains a leading cause of serious neonatal infection despite the efforts made on prevention and profilaxy. With a wide range of pregnant women being colonized (10-30%), despite universal prenatal screening and prophylaxis, a high incidence of neonatal sepsis was reported. In our centre, we stated a 1% neonatal sepsis incidence in the year of 2008, so we decided to investigate this neonatal sepsis and it’s relationship with group B streptococcus.

Material and methods
We analyzed the clinical records of the neonates admitted to Neonates Intensive Care Unit in the year of 2008 and of its mothers, and crossed the data with the records of the GBS screening realized in our centre. Statistical analysis was realized with SPSS 16.0 software.

Results and discussion
In the year of 2008 we had 3125 births, with 28 neonatal cases of sepsis, of which 50% corresponded to preterm births, with only one confirmed infection by GBS. We stated 7 cases of infection by other bacteria, and the remaining had no cultural diagnosis of causal agent (72%). In almost 50% of the cases the delivery was by caesarean section, with 14% of VLBW neonates. In the majority of cases, gestational age was less than 35 weeks, so screening for GBS hadn’t been done yet.

Conclusion
Despite the importance of the GBS and the 1% incidence of neonatal sepsis, the overall incidence of diagnosed infection with this GBS agent was low. More accurate diagnosis is necessary to achieve final conclusions.

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Evolution of perinatal early-onset sepsis and group B Streptococcal infection in the period 1998-2008

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Background: Early-onset sepsis (EOS) and GBS infections cause a high morbid-mortality in neonates. The infection rate varies and our aim was to assess the evolution of infection indexes before and after the implementation of GBS screening (GBS-S) in pregnant women.

Subjects and methods: In a population of 28,049 consecutive livebirths (LB), the EOS rate due to any microbe, GBS bacteraemia (GBS-B) rate, positive cord blood culture (P-CBC) and overall CBC done as well as number of VLBW (<1500g) have been done in three periods: before starting GBS-S, period I (1998 – 2001), at the beginning of GBS-S, period II (2002 – 2004), and at the full implement of GBS-S, period III (2005 – 2008).

Results: In periods I/II and III, EOS/1000 LB rate increased steadily (1.16 / 1.86 / 2.32), and GBS-B /1000 LB rate reached an upper level in period II and decreased thereafter (1.0 / 2.1 / 0.9). The rate of (P- CBC) /1000 LB also rose through the three periods (1.2 / 3.8 / 4.9). The overall CBC /1000 LB done also increased in the three periods (1.2 / 3.8 / 4.9) as well as number of VLBW (71/ 101/ 131). There were none death due to EOS.

Conclusions: Over an 11-year period the rate of EOS has risen steadily according to increment of VLBW infant births. Incidence of GBS-B remained at a low rate. Early use of prophylactic antibiotics in neonates with infection risk factors is responsible for the null mortality registered.

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Frequency of group B streptococcus colonization/infection among diabetic and nondiabetic pregnant women

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Objective: Pregnancy and diabetes mellitus are risk factors for genital infections, related to potential glucosuria and immunologic dysfunctions. This study was undertaken to compare the frequency of group B Streptococcus (SGB) colonization and infection in diabetic and nondiabetic women during pregnancy.

Patients & Method: Five hundred and sixty-one patients were included in this retrospective analysis between 2004 and 2006. They were stratified into 3 groups: group I: 31 pregnant women with previous diabetes mellitus; group II: 230 pregnant women with gestational diabetes; and a control group (group III) of 300 nondiabetic pregnant women. Culture specimens for SGB were obtained from lower vaginal walls and anus between 35 and 37 weeks of gestation, unless there was documented urinary tract infection by the same agent earlier during pregnancy. Statistical analysis was performed using SPSS 15.0 for windows.

Results: The SGB colonization rates were 12.9% and 12.2% in group I and II, respectively. No significant difference was found when they were compared isolated to the control group (12.7%). In addition, there was no significant difference in the frequency of urinary tract infection caused by SGB between group I (3.2%) and II (2.6%), or when compared to group III (2.0%).

Conclusion: Although maternal diabetes mellitus was considered as a risk factor for group B Streptococcus colonization during pregnancy in some series in the literature, this maternal condition doesn’t appear to be associated to a higher frequency of SGB colonization or urinary infection rate in our pregnant diabetic population.

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Group B Streptococcal colonization rate in Korean pregnant high risk women

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Objective: To evaluate the colonization rate of the group B streptococcus (GBS) in Korean pregnant high risk women, and the antimicrobial susceptibility of isolated GBS.

Background: GBS, also known as Streptococcus agalactiae, constitutes one of the leading pathogens associated with both early and late-onset neonatal sepsis. And preterm delivery or late-onset sepsis cannot be completely prevented, and emerging antibiotic resistance has become a major concern in many countries.

Methods: From July 2008 to December 2008, 158 pregnant women who visited our high risk pregnant clinic for antenatal care after 35 weeks of gestation were enrolled. According to Centers for Disease Control and Prevention (CDC) guideline for collecting and processing clinical specimens for GBS culture, specimens were obtained from the lower third of the vagina or urine, and then inoculated on Todd-Hewitt broth. The test for antimicrobial susceptibility was performed by a disc diffusion method.

Results: The 9/158 (5.7%) pregnant women, 8/113 (7.1%) had a positive culture from urine sample and 1/45 (2.2%) from vaginal culture. The antibiotic resistance rate was 5/9 (55.6%) for erythromycin and 7/9 (77.8%) for clindamycin.

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Epidemiology of Neonatal Group B Streptococcal infection in Portugal

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Group B Streptococcus (GBS) may cause severe neonatal infection. Former 4 years Portuguese study, has given an insight on proven infection. However suspected cases were not included giving a false knowledge on the true incidence of disease. Moreover, despite no national policy, GBS screening and prophylaxis is done all over the country. Aim: To evaluate the true burden of streptococcal neonatal infection and to assess the effect of screening. Design: National epidemiologic surveillance. Methods/ Patients: From January 2006 through December 2007, systematic, voluntary, national surveillance was performed. Septic infants <90 days with GBS positive culture in any site – blood, CSF, joint, gastric or tracheal aspirate, peripheral swabs or positive antigen - were enrolled provided no other bacteria had been isolated in blood culture. Results: 70 cases were reported - incidence 0.34/1000LB. From them, 46 had positive blood culture – incidence for proven infection 0.22/1000LB vs. 0.54/1000LB in the former study. The inclusion of non-proven infection add 39% and 80% more cases respectively in the first and second years of the study as if only proven cases had been included. In early-onset infection group 42% of neonates were born by caesarean section; 61% of mothers had been screened and 46% of them were negative; amongst the positives 37% were given full prophylaxis. Conclusion: Enrolling newborn infants with suspected GBS infection give a new insight on the true burden of disease. Screening and prophylaxis decreased the incidence of disease but are far from being the best way to control it.

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Prevalence of group B streptococcal colonization in pregnant women and their newborns, preliminary results

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Pregnant women who are group B streptococci (GBS) carriers have the potential to transmit the organism to their newborn infants. There is a spectrum of maternal and fetal GBS infections ranging from asymptomatic colonization to sepsis. GBS (streptococcus agalactiae) is a main cause of perinatal infections and neonatal sepsis and meningitis. As prevalence of GBS varies from place to place the present study was carried out to measure it in pregnant women at term and their neonates in our unit.

Objective: This study was done to evaluate the prevalence of rectovaginal colonization with GBS among pregnant women who delivered in our center and the transmission rate to their babies.

Material and Methods: Rectovaginal cultures were obtained from 487 pregnant women with gestational ages greater than 25 weeks and further samples were gathered and from the external ear of their newborns. The subjects were admitted to the labor room of Attikon University Hospital from September 2008 to February 2009. The study is ongoing.

Results: Out of the 487 women who were evaluated for GBS, 35 (7.2%) had rectovaginal colonization. 18 neonates out of 478 (3.76%) had positive B streptococci cultures with a transmission rate of 52.94% with a transmission rate of 62.5% among women who delivered vaginally and 22.2% with CS.

None of the neonates developed early-onset B streptococci sepsis.

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The incidence of B group Streptococcus among women in pregnancy and delivery in Latvia

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Introduction: B group streptococcus (BGS) still remains the main cause of neonatal sepsis and maternal BGS colonisation is recognized as the main risk factor in development of neonatal sepsis. 5 - 30% of pregnant women in European countries have rectovaginal colonization with BGS. If women is BGS positive, the risk for newborn infection is 30-70% and 0.5-1 of 1000 infected newborn develope early neonatal sepsis. It is approved that antibacterial prophylaxis during delivery decrease the risk 3-4 times. But the approach of antibacterial prophylaxis depends on BGS incidence among women in pregnancy and delivery. The BGS incidence in Latvia is not estimated and current recommendations of antimicrobial prophylaxis is based on risk factors during delivery.

Objective: Our aim is to estimate the incidence of BGS among women in pregnancy and delivery in Latvia to recommend appropriate approach of antimicrobial prophylaxis during delivery.

Methods: In study were included 100 women from 35 to 37 weeks of pregnancy whom we examined the culture for BGS by swab from low vaginal part and rectum and 15 patients with premature labor whom we examined culture for BGS and RT PCR with Gene Expert System BGS.

Results: we found that 25% of women from 35 to 37 weeks of gestation are BGS positive.

Conclusion: Our data supports that current approach of antimicrobial prophylaxis during delivery in Latvia has to be revised. All pregnant women has to be informed about BGS, explained the consequences and recommended to examine culture for BGS during pregnancy.

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Isolation of common pathogens in cases of vaginitis

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Aim: To register the frequency of pathogenic microorganisms which were isolated in the cultivations of vaginal samples in women with symptoms of vaginitis.

Material-Method: During 18 months 262 vaginal samples of women aged 18-65 years with symptoms of vaginitis, were examined. For their culture blood agar, McConkey, Sabouraud and Gardnerella were used and then followed their identification.

Results: In 108 positive samples (41.2% of the total examined) the following pathogens were isolated:

A) Candida spp: 59 samples percentage 54.6%
B) Gardnerella vaginalis: 28 samples percentage 25.9%
C) Trichomonas vaginalis: 9 samples percentage 8.3%  D) Candida spp + Gardnerella spp: 5 samples, percentage 4.7%
E) Candida spp + Trichomonas vaginalis: 7 samples percentage 6.4%

85% (in total 50 samples) of the samples with Candida spp regarded the Candida albicans.

Conclusions: 1) The Candida spp and more particularly the Candida albicans represented the most frequent cause of vaginitis (65.8% of the positive samples). 2) The Gardnerella vaginalis, although considered in the bibliography as the most common of the causes of vaginitis, in this study appeared only in 30.6%.

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**HIV infection and pregnancy: obstetric and neonatal outcomes**

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**Objective:** To assess maternal, obstetric and neonatal outcomes in pregnant women with HIV infection.

**Patients & Methods:** A retrospective analysis of 32 pregnancies with HIV infection followed at our centre between 2004 and 2008 was performed. Data on maternal demographic profile, evolution of HIV infection during pregnancy, obstetric complications, type of delivery and neonatal outcomes were analyzed.

**Results:** Mean maternal age was 30 years. HIV infection was diagnosed during pregnancy in 13 women, while amongst others, the mean interval between diagnosis of HIV and pregnancy was 6.3 years. Fifteen patients had high viremia (>1000 copies/ml) in the first trimester; 30 were medicated with zidovudine during pregnancy. First trimester miscarriage rate was 6.3%. One termination of pregnancy was performed for anhydramnios. In 6 cases (20.7%) intrauterine growth restriction was detected. Preterm delivery rate was 27.6% (8 cases) and premature rupture of membranes occurred in 2 cases (6.9%). Twenty-six (89.7%) patients had peripartum chemoprophylaxis with zidovudine. Caesarean rate was 93.1%. Eight neonates (27.6%) were small for gestational age, 2 of which resulted from pregnancies complicated with advanced maternal infection, and 4 resulted from mothers with drug addiction and other sexually transmitted diseases. No cases of congenital HIV infection were detected.

**Conclusion:** HIV infection is frequently associated with drug abuse and sexual promiscuity so that sometimes it becomes difficult to predict the independent impact of HIV infection in pregnancy and neonatal outcomes. Fortunately, no case of vertical transmission of the disease was recorded, in spite of our small population size.

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Pilot study about evaluation of feasibility and acceptability of HIV-rapid screening test during labor in pregnant women with unknown serological HIV status

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One of the Northern Region in Italy, Lombardia, has the highest incidence of AIDS cases (6/100.000 residents). Brescia has the highest incidence of AIDS cases per province. Clinical unpublished data reported about 300 new case of HIV in Brescia, with a prevalence of HIV infection of 0.1%. We supposed that 5% of pregnant women in labor have an unknown HIV serological status (UHS). The aim of these study was to assess the acceptability and feasibility of a rapid HIV screening test both for patients and for medical practitioner. From December 2007 to December 2008 48/2750 pregnant women during labor were elegible for the study: 26 were recruited (54.2%), 2 didn’t accept the test. The 24 rapid test evaluated had a negative Result, confirmed with Western Blot (WB) three month after delivery. Acceptability of the test was very high for patients (92.3%) and surprisingly quite low for medical practitioner (54.2%). Causes for not recruit patients were: ethnic status (Italians vs. strangers pregnant; 75 vs. 50%); evidence of adequate prenatal care (75 vs. 68%); labor during night hour (58 vs. 36%); advanced stage of labor (25 vs. 9%). Pregnant women elegible for the study were 2%, less than expected: UHS pregnant with planned caesarean section were excluded because attended WB the day before surgery. Preliminary data confirmed the acceptability of the test. Further data are necessary to evaluated cost-effective of this procedure to detect UHS pregnant at high risk of MTCT, the one who usually received inadequate or no prenatal care.

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Register of HIV rapid testing 2007-2009

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Objective: To determinate the incidence that HIV rapid testing are applied for, in delivery room, and their Results during the period January 2007 to February 2009.

Patients and Methods: Observational retrospective study about the incidence of patients who required an HIV rapid testing (Determine HIV ½ - Inverness medical) in delivery room during the study period. The recommendations to apply for this test were: women delivering with no prenatal care or without HIV serology. All positive Results were confirm in second time by EIA testing.

Results: During the study period we made 803 HIV rapid testing to pregnant women who were admitted in delivery room (5.50%). The distribution by years was 336 in 2007 (4.73%), 428 in 2008 (6.23%) and 39 in 2009 (3.29%). We identified four positive HIV rapid testing (0.49%) and confirmed the Results in only one case by EIA testing and in second time by Western Blot.

The predictive positive value (PPV) in our center was 25%, with a sensibility of 100% and specificity of 97%.

The delivery mode we chose in three cases was elective caesarean section, with infusion of Zidovudine, and the only case of vaginal delivery was a precipitated delivery without infusion of intravenous zidovudine.

The only positive Result was in a no prenatal care pregnancy without HIV serology in first trimester, with an elective caesarean section. We didn’t identified mather- to- child transmission.

Conclusions: The PPV in our center was 25%, which is less than published in literature.

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“Mitochondrial toxicity in HIV infected pregnant women and its association with adverse perinatal outcomes”

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HIV infection and highly active antiretroviral treatment (HAART) increase risks for adverse pregnancy outcomes. Nucleoside analog reverse transcriptase inhibitors (NRTIs) are known to inhibit mitochondrial DNA (mtDNA)polymerase NRTIs and HIV infection itself can cause mitochondrial dysfunction.

Objectives: To study the association between mtDNA content and pregnancy outcomes. To assess the impact of HIV infection and HAART on the mtDNA.

Study Design: mtDNA content was determined by PCR in maternal peripheral blood mononuclear cells (MPBMC), umbilical cord blood and placenta from 27 HIV infected women and 24 non infected.

Outcome measures: perinatal mortality, prematurity, small for gestational age, birth-weight and low Apgar score.

Results: HIV-infected women showed significant adverse pregnancy outcomes when compared with uninfected controls: 44% (12/27) versus 12.5% (3/24) (OR 1.48, 95% CI [1.043-2.090]). No significant correlation was found between mtDNA content and adverse pregnancy outcomes. mtDNA content of MPBMC, fetal cord blood and placenta was similar in both groups.

At delivery HIV infected women showed significant MPBMC mtDNA depletion when compared with non infected pregnant (38% mtDNA decrease, P<0.05). This MPBMC mtDNA depletion was even greater on NAÃVE pregnant when compared with HIV infected pregnant on HAART (55% mtDNA decrease, P=0.05).

Conclusions: MPBMC from HIV-infected women show decreased mtDNA content at delivery. This depletion was much higher in NAÃVE patients who started HAART in the second trimester than in patients who previously had received HAART. Further studies are needed to better understand morbidity associated with exposure to HAART during pregnancy and mitochondrial toxicity.

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Reflections on the unrelenting prevalence of maternal hepatitis B infection in a high endemicity area – What have been overlooked?

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Objective: To examine the prevalence of maternal hepatitis B (HBV) infection in the past ten years, and the age- and parity-specific incidences, for evidence of control of HBV infection in the female reproductive population.

Research Design and Methods: A retrospective cohort study was performed on 58,736 consecutive pregnant women delivered from July 1998 to June 2008. Maternal HBV status and demographic data were retrieved from a computerized database for analysis by year, age, year of birth, and parity.

Results: A total of 5,788 (10.1%) women had HBV infection, and the annual prevalence was around 10% throughout. When categorized by maternal age into six 5-years cohorts, the incidence increased from 6.8% in the <20 years cohort to 10.8% in the 20-24 & 25-29 years cohorts, then declined to 9.3% in the ≥40 years cohort (p<0.001). When categorized by year of birth into 5-years cohorts, the incidence varied from 9.2% for the 1965-1969 cohort, to 11.3% in the 1980-1984 cohort, then declined to 7.3% in the ≥1985 cohort (p<0.001). Multiparas had higher incidence when compared with nulliparas overall (10.5% versus 9.6%, p=0.001), and significantly higher incidences for the 25-29 year (p=0.009), 30-34 year (p<0.001), and 35-39 year (p=0.032) cohorts when analyzed by year of birth.

Conclusions: The prevalence of maternal HBV infection remained constant at 10% for the past decade. The changes in relation to age and parity suggested that horizontal transmission, probably by sexual contact, had played an important role in maintaining the same prevalence as reported here 20 years ago.

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Changes in frequency and causes of sepsis in newborns in period of wide utilisation of antibiotics during delivery

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Introduction: Frequency of main pathogenic species causing neonatal sepsis is under constant changes. Therefore, we have to evaluate these changes and give some recommendations for proper antibiotics treatment.

Aim of Study: The aim of retrospective study was to determine if there are any changes (concerning type of micro-organism) causing of sepsis of newborn in our Centre during the period 2004-2008.

Method: We took an overview of newborns under 7 days of life with positive liquor culture and hemoculture (Streptococcus B, E. coli)

We examined mortality of newborns infected E.coli, percentage of term- and pre-term newborn, percentage of mortality of newborn under 33 wk gestation age.

Is there any changes in incidence concerning type of pathogen spp.?

In what percentage mothers were treated by antibiotics, and which one?

We examined positive predictive factors of risk, specially concerning: small gestation age (under 33 wks), febrile state during delivery, rupture of membrane lasting more than 18 hrs.

One of main aims of our study was to examine if there is any connection between antibiotics treatment during delivery and increasing incidence of E. coli and Ampicillin-resistant infection.

Results: As a Result of our study, we found that E. coli was dominant cause of sepsis in newborns. In 58% of newborn from our study group we had a positive hemoculture, followed by increased parameters of bacterial infection.

Gram negative spp. caused 62%, and Gram positive 38% cases of sepsis of newborn.

Pathogen species were sensitive on Amikacin 73%, imipenem and meropenem 90%.

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Is antenatal Toxoplasma gondi screening during pregnancy necessary in Timisoara, Romania?

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Introduction: A primary antenatal Toxoplasma gondi infection could generate fetal malformations. Only non-immunized or gravidas with immunodeficiencies are at risk to transmit the agent to the fetus if an infection occurs during pregnancy. Aim of the study: To analyze the percentage of gravidas who are immunized for Toxoplasma gondi at the time of the pregnancy.

Methodology: From 31.07.2007-1.05.2008, 660 gravidas were tested for the presence of IgG/IgM anti-Toxoplasma gondi antibodies. The gravidas were grouped according to age and to domicile. The percentage of immunized gravidas was calculated for each subgroup.

Results: From 660 gravidas 308 were positive for IgG-anti-Toxoplasma gondi antibodies while 352 were negative. The age of gravidas varies from 15 to 40 years; 308 gravidas live in urban and 190 in rural areas. The overall percentage of gravidas immunized to Toxoplasma gondi before pregnancy was 46%. The percentage of immunized gravidas is higher in rural than in urban areas independent of the age of the gravida. Out of 660 gravidas only 12 had a positive IgM-anti-Toxoplasma gondi antibodies titer, 8 coming from urban areas. No fetal infection was found in our study.

Conclusion: Around 54% of gravidas don’t have a Toxoplasma gondi infection before pregnancy and could be infected for the first time during pregnancy. The percentage of gravidas susceptible to receive a primary infection during pregnancy is higher in the urban than in the rural areas. Although we didn’t detect any fetal infection in our study we recommend the screening test for all the gravidas.

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Prevalence of human papilloma virus infection in pregnant turkish women; comparison with non-pregnant

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Purpose of Investigation: We aimed to find prevalence of Human papilloma virus (HPV), to define the 100 genotypes and subset of 14 oncogenic genotypes in pregnant Turkish women and compare these with non-pregnant women.

Methods: Cervical thin-prep specimens were obtained from 164 women in first trimester pregnancy and 153 women without pregnancy.

Results: 29.2% of pregnant versus 19.6% of non-pregnant Turkish women have at least one of the 100 types of HPV infection, difference was statistically significant. The rate of 14 high-risk HPV genotypes infection was significantly higher in pregnant (14.6) compared to non-pregnant Turkish women (9.6%).

Conclusions: Pregnant Turkish women is under higher risk for all HPV infection including 14 high-risk for servical cancer genotypes.

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Effects of Nematodosises and Giardiasis during pregnancy

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Such widespread infections as Ascariasis, Toxocariasis and Giardiasis are often elude observation during pregnancy. However their effects on mother’s and fetus health and immunity are significant.

158 pregnant women were under supervision during 2006-2008 yrs. 49 of them were infested with Ascaris lumbr., Toxocara canis or Lamblia intestinalis. 28 women have Giardias without clinical symptoms, and 81 had no researched infections. In previous obstetrical history the infested women have had the unsuccessful term more often (29.6±1.8%, 6.3±2.6%, 6.8±1.5%). In the first trimester of this pregnancy the threat of a spontaneous abortion in the 1st group was higher also (42.9±1.1%; 28.6±1.8; 23.5±0.9; p<0.05). The early gestosis have 55.1±1.0% of the infested women, 57.1±1.6% - Lambliasis carrier, 35.8±0.7% - non-infested (p<0.05). The anemia (40.8±1.1), hydramnion (26.7±1.7), premature birth (26.7±1.7) was observed in the 1st group statistically more often. 22.4±1.3% of infested mothers have respiratory and skin allergic symptoms and only 8.6±1.0% in the control group.

The newborns had suffered from mother’s infection in such ways: intrauterine growth retardation (19.2±1.3%; 12.5±2.0%; 5.6±1.2%; p<0.05), fetal hypoxia (36.7±1.6%; 26.7±2.6%; 10.3±1.8%; p<0.05), meconium in amniotic fluid (36.7±1.6%; 33.3±2.5%; 10.3±1.8%; p<0.05); cord entanglement (36.7±1.6%; 13.3±2.6%; 10.3±1.8%; p<0.05). Pelvic presentation in the 32-34 week of pregnancy was in 31.8±1.3% cases in the 1st group.

The observed findings show that Nematodosises and Giardiasis during pregnancy are the risk factors of obstetrical and perinatal pathology. The risk of allergic pathology is increased also.

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The prevalence of Leptotrichia amnionii sp. nov. in pregnant women

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Introduction: Leptotrichia bacteria belong to the group of Gram-negative anaerobes most frequently colonizing the oral cavity and reproductive organs. Leptotrichia sanguinegens constitute one of the bacterial factors in postpartum bacteremia of mothers and newborns, whilst Leptotrichia amnionii sp. nov., described for the first time in 2002, has turned out to be the etiopathogenetic factor in missed abortion in the second trimester of pregnancy.

Aim: The purpose of this study was evaluation of the frequency of occurrence of Leptotrichia amnionii sp. nov. in patients in the 1st, 2nd and 3rd trimester of pregnancy. Materials and methods: The study involved 121 patients. Amplification reactions detecting the presence of Leptotrichia amnionii sp. DNA in the smears were performed using specific starters complementary to gene encoding 16SrRNA of Leptotrichia amnionii - primer 1 Lam upper and primer 2 Lsp lower – complementary to Leptotrichia 16SrRNA. After amplification, the specimens were placed on 1% agarose gel in the presence of MassRuler marker (Fermentas). Next, PCR products were ligated to pGEM-T Easy Vector and then competent E. coli DH5α cells were transformed with pGEM vector with an insert. Plasmid DNA isolation was performed using Plasmid Mini kit from A&A Biotechnology. Results: In the group of 121 pregnant patients Leptotrichia amnionii sp. nov. was identified in 14 women, which is 11.57%.

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Assessment of Amniotic Erythropoietin (a-Epo) and Troponin-T (a-TnT) levels in Parvovirus-B19 infected fetuses

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Background: Apoptosis of the erythroblasts and the myocardial cells can lead to severe anemia, cardiac failure and fetal death in B19-infected fetuses. Reflecting apoptosis, amniotic erythropoietin (a-Epo) and Troponin-T (a-TnT) levels are known to increase. In this study, a-Epo and a-TnT levels were measured to analyze the degree of hypoxia and myocardial damage in B19-infected fetus.

Method: Among 14 pregnant women infected with B19, five cases were symptomatic; fetal edema, ascites, and the remaining were asymptomatic. Immunoglobulin injection into fetal abdominal cavity; IFAC (2g/kg) was performed in four symptomatic cases. Amniocentesis was performed in every 14 women under informed consent, in four symptomatic cases taken prior and subsequent to IFAC. Amniotic B19-DNA, a-Epo and a-TnT levels were measured.

Results: In five symptomatic cases, two cases were surviving by IFAC. The amniotic B19 DNA level reflected the clinical state of the fetus. In three dead cases, the a-Epo and a-TnT levels were more than 100 mU/ml and 200 fg/ml, respectively. The a-Epo levels for two surviving cases of symptomatic fetuses decreased from 87.4 mU/ml to 34.6 mU/ml and 44.2 mU/ml to 29.3 mU/ml, while the a-TnT levels decreased from 200 fg/ml to undetectable levels. The a-Epo levels in the asymptomatic cases were 20.9±15.3 mU/ml (Mean±S.D.), and the a-TnT levels were undetectable.

Conclusion: All infected woman were showed positive B19-DNA level in amnion. Fetal conditions were reflected with a-Epo and a-TnT levels. Both a-Epo and a-TnT can be valuable to understand in the fetal clinical condition.

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An audit on the impact of ANTT (Aseptic Non Touch Technique) in reducing the infection rates in preterm neonates with central lines

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Background: ANTT has been implemented in several hospitals across the NHS in an attempt to reduce the infection rates based on evidence from adult studies. There is currently no published data on its effectiveness in newborn babies. ANTT was implemented in the Regional Neonatal Unit at our Trust in January 2006 as part of a Trust wide policy.

Aim: To assess the impact of ANTT in reducing the infection rates in neonates with central lines.

Methodology: We undertook a retrospective case note review of the long lines (peripherally inserted central catheters or PICC lines) in preterm infants admitted to the tertiary neonatal unit at our Trust. Preterm babies with long lines were identified by reviewing case notes of those receiving TPN and/or inotropes. The infection rates in the babies born during the pre ANTT period (Jan 2005 to Dec 2005) were compared with those born during post ANTT period (July 2006 to July 2007).

Confirmed infection was defined as presence of clinical suspicion plus CRP >10 and a positive blood/CSF/urine culture with significant growth of a single organism.

Results: Overall, 178 long lines were reviewed; 90 were from pre-ANTT period and 88 from post-ANTT period. Both groups were comparable.

Confirmed infection rate has fallen from 26.6% (pre ANTT) to 19.3% (post ANTT). One baby had died in each group as a direct Result of sepsis.

Conclusion: ANTT is effective in reducing the incidence of confirmed infection or bacteraemia in preterm infants with long lines.

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New treatment of fetal cytomegalovirus infection with immunoglobulin into fetal abdominal cavity: three case reports

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Congenital cytomegalovirus (CMV) infection causes gravely adverse outcome such as neurologic and mental disorders. In late years, there are some reports that immunoglobulin is given to the pregnant mother or the amniotic fluid for symptomatic CMV infected fetuses, which reported good effect. IFAC: Immunoglobulin injection into fetal abdominal cavity (2g per 1kg in estimated fetal weight) was performed for three cases of symptomatic CMV infected fetuses in our hospital. Four times of IFAC were performed for three cases.

The representative case was 22 years old of primipara. Fetal ascites and hepatosplenomegaly were clearly found in 22th weeks’ gestation. CMV-DNA was detected in amniotic fluid (2.4×10^7 copies/ml). IFAC was performed in four times once a week. The fetal ascites disappeared in 33rd weeks, but CMV-DNA in amniotic fluid did not decrease (2.7×10^7 copies/ml). Erythropoietin in amniotic fluid was 3,690mU/ml, which was suggested the presence of extensive acidosis. A 1,128g boy was delivered by caesarean section at 33rd weeks. After delivery, Platelet transfusion and ganciclovir administration were performed intermittently. Two years later, deafness and development retardation are not noted. CMV-DNA in amniotic fluid decreased neither three cases, but other aspects as neurological, physical and mental development were normal.

IFAC can lead to continue immunoglobulin action, which does not change fetal blood circulation suddenly. Lifesaving of serious cases with congenital CMV infected fetus and improvement of newborn infant consequence are possible under an appropriate pediatric treatment following IFAC.

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**Congenital Syphilis, the resurgence of a former disease. Case report**

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Congenital syphilis is one of the most devastating causes of perinatal morbidity and mortality. Although the majority of cases are seen in developing countries, they also occur in the developed ones. In these countries the re-emergence of infectious syphilis (primary, secondary, and early latent) has led to the rise of congenital syphilis. In spite of being a severe disease, congenital syphilis can be preventable. Antenatal serological screening is an important measure to reduce vertical transmission of syphilis, since effective treatment is available, but its delivery depends on identifying infected women. Parental penicillin G is the only therapy with documented efficacy for syphilis during pregnancy. Maternal infection is entirely treatable with penicillin which also prevents the sequelae of miscarriage, preterm delivery, neonatal death and congenital infection (with its long term morbidity). Over the last years, three cases of congenital syphilis were identified in our unit. One of the cases is reported in this essay - a 25-year-old woman, G2 P1 (VDRL nonreactive earlier in the pregnancy). At 31 weeks’ gestation an ultrasound showed hydrops fetalis. Mother’s syphilis serology was performed (VDRL 1/64; FTA abs +). At 32 weeks’ gestation a syphilis-infected boy was delivered (VDRL 1/32; FTA abs +; abnormal CSF). Anaemia, thrombocytopenia, hepatoesplenomegaly, jaundice and radiographic evidence of bone disease were present in the newborn. Because of the serious consequences of congenital syphilis and as it is preventable and treatable continued screening of all pregnant women is vital.

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The Contribution of Perinatal Infection to Acute Lung Disease in Premature Neonates

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Background
The role of perinatal infection in acute lung disease (ALD) of premature neonates was studied using Bronchoalveolar Lavage (BAL) specimens obtained from Flexible Bronchoscopy (FB) in neonates with ventilator dependant ALD.

Methods
24 premature neonates (GA: 28-36 weeks) with ventilator dependant ALD <10 days, clinically stable with no signs of sepsis, were recruited. Flexible Bronchoscopy (2.8mm) was performed as described by Wood. BAL specimens (x2) obtained from R and L bronchi were processed for typical, atypical organisms and viruses. Concurrent blood cultures were obtained. Parental consent preceded the procedure.

Results
14/24 (58%) neonates were delivered by Caesarean section. Pregnancies were not complicated by prolonged rupture of membranes (<24hours) or maternal infection. The neonates had WCC 8.8±3.9 (m±sd); platelets 201±104; CRP 17±33.8mg/l. The Blood culture was positive in 8/24 (33%); (6xstaph species; candida; acinetobacter)
Only 4/24 neonates (17%) had positive BAL cultures (Staph species, Klebsiella, Acinetobacter, CMV)

Conclusion
FB is a safe procedure in sick but stable neonates.
4/24 neonates had positive BAL cultures, 3 bacteria and 1 virus; the bacteria were nosocomial; the virus isolated was acquired (CMV IgM negative). Perinatal organisms were not isolated in any BALs. The neonates were not septic; WCC and CRP being within normal range. 33% postive blood culture were probably nosocomial (staph species). There was no correlation with positive BALs. The Results indicated that infection, both perinatal and congenital, plays a MINOR role in the pathogenesis of ventilator dependant ALD in neonates <10 days of age.

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Pregnancy outcome and maternal complications in women with chronic hypertension

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Aim: To evaluate the pregnancy outcome and maternal complications in 166 pregnant women with chronic hypertension. A correlation between specific clinical features and various risk factors was made.

Methods: Onehundredsixtysix pregnant women with hypertension in pharmacological treatment before pregnancy or evidence of hypertension that needed a pharmacological treatment before the 20th week of gestation in the actual pregnancy were evaluated.

Results: Fifteen patients (9%) developed preeclampsia. Thirteen deliveries (7%) were induced because of a significative rise in blood pressure and 5 women (3%) had placental abruptio. Twenty-four infants (14.6%) were LBW, 13 were VLBW (7.9%) and 35 (21%) were SGA, but only 8 (5%) showed a growth restriction in utero. A statistically significant correlation between the systolic blood pressure at the first control and IUGR (1% if PAS<140mmHg vs. 9% if PAS>140mmHg), between abnormal uterine artery Doppler velocimetry and development of superimposed PE (37% if abnormal vs. 5% if normal), IUGR (16% if abnormal vs. 1% if normal) and LBW (63% if abnormal vs. 13% if normal) was found. Other maternal factors (age, geographical origin, presence or absence of kidney diseases, smoking and an abnormal fundus oculi) were not correlated with maternal and fetal complications.

Conclusions: In pregnant women with chronic hypertension, the incidence of maternal and fetal complications was found to be higher than in the general population, but lower than that reported in the literature. A systolic blood pressure higher than 140mmHg at the first control was correlated with an increased incidence IUGR.

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Predisposing factors for preeclampsia in twin pregnancies

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Objective: To identify predisposing maternal factors for preeclampsia in twin pregnancies and to find weather twin pregnancies following in vitro fertilization (IVF) increase the risk of preeclampsia.

Material and Methods: A retrospective case control study of preeclampsia in twin pregnancies was performed. Maternal characteristics were evaluated. Patients' data were obtained from a computerized database at the University clinic of Ob/Gyn in Skopje. The data from the period January 1st, 2000 to December 31st, 2008 were analyzed using SPSS statistics. Results: During the study period there were 741 twin deliveries. 4.2% of the women giving birth were admitted at our hospital at least once with diagnosed severe preeclampsia and 7.5% with mild preeclampsia. Patients with severe preeclampsia were more often primiparous, younger than 35, gave anamnestic data for chronic hypertension, were diagnosed diabetes mellitus (preexistent or gestational), conceived following IVF treatments. Twin discordancy was noticed to be associated with severe preeclamptic patients more likely than with patients with mild preeclampsia and normotensive ones. In 72.5% of the women with severe preeclampsia all of our investigated risk factors were present. In multivariate analysis parity, IVF treatment and maternal age, appeared to be independent risk factors for the development of preeclampsia. Conclusion: IVF treatments in primiparous patients and age younger than 35 years are independent risk factors for preeclampsia. We determined twin discordancy as an extra independent risk factor for the occurrence of preeclampsia.

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Analysis of the quality of the prenatal assistance to hypertensive pregnant in the South region of São Paulo’s municipal district in 2008

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As Pregnancy-induced hypertension (PIH) has high incidence and causes serious consequences, an adequate program of maternal health during the prenatal period has an extreme importance. The PIH is frequently related to maternal and perinatal mortality. Thus, the prenatal health care must be stimulated since the beginning of the pregnancy, helping identify risk factors and promoting preventive actions. The purpose of this study is to evaluate the quality of the medical assistance during the prenatal period to pregnant with PIH, in the South Region of São Paulo’s Municipal District in 2008. This purpose was accomplished by developing a transversal study, survey-like. A questionnaire was applied to each PIH pregnant studied, after her signature to a Free and Informed Consent. Subsequent to collecting data, the Results were organized and computed table-form by Epilinfo software. As a result to the questionnaire applied, a high level of unexpected pregnancy (70%) was obtained, enabling an association with the low level of scholarity (44.2% without primary education) of the pregnant involved. Furthermore, although 95% of pregnant referred having a partner, most were not married, disclosing the lack of family planning and the high quantity of unexpected pregnancies, contributing to miscarriages and stillborns (28.1%). In addition, a low percentage of pregnant (35%) had attended the preconized number of prenatal consultations, however, the majority of them were aware of the importance of the prenatal care. This suggests that the problem is not only a matter of public health but also involves the poor educational system implemented.

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Ambulatory management in high risk preeclampsia patients

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Objective: To determine the utility and efficacy of the ambulatory management of the patient with Preeclampsia in Expectant Management diagnosis

Methods: Patients with Preeclampsia diagnosis, between January and December 2008, with in hospital management for 7 days and posterior ambulatory care and follow up:

Home – Hospital Ambulance transportation, daily home vital signs control made by a nurse, once a week control with the High Risk Gynecologist for clinical vigilance, platelet count and ultrasound biophysical profile, plus once a week Fetal Doppler and every three weeks a Fetal Weight Estimation, patient education on warning signs for seeking urgent medical attention, the integral management of the patient is made in coordination between the OB GYN department and the patient’s Health Maintenance Organization.

Results: Twenty four patients were studied, 21 of them had single pregnancies with Mild Preeclampsia, 3 had Twin pregnancies with Mild Preeclampsia and 2 pregnancies with Preeclampsia associated with Chronic Hypertension. Three of the 24 patients progressed to Severe Preeclampsia, 1 patient developed HELLP Syndrome and 2 patients with Preeclampsia associated with Chronic Hypertension presented unstable Blood Pressure measurements. Six patients had premature deliveries and all patients had healthy new born babies. A 100% adherence to the plan was observed, and no complication was related to the ambulatory management.

Conclusion: We consider that ambulatory care is a safe option for these type of patients, without augmenting maternal/fetal morbidity and mortality. It's important to study such experience in a larger group of patients.

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Morphometric characteristics of testes in fetuses and newborns from mothers whose pregnancy was complicated by pre-eclampsia

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Pre-eclampsia influence on the structure of testes in fetuses and newborns was investigated using morphological techniques. The changes in the number and area of seminiferous tubules (ST) were revealed. Observed cases were divided into some groups: P 1, P 2 and P 3 (first-, second- and third-degree pre-eclampsia). Fetuses and newborns from mothers with physiological pregnancy have been included into the control group. In control group the average number of ST (22.02±0.32) in the limited field of vision (LFV) was maximal (Â<0.001) among all groups. The average area of ST – (1.23±0.01) m²×10⁻⁹, was less (Â<0.001) than analogous index in group P 1 and more (Â<0.001) than that in groups P 2 and P 3. In group P 1 the average number of ST in the LFV has been reduced relatively to the control group and was 18.57±0.25 (Â<0.001). The average area of ST has been enlarged to (1.47±0.02) m²×10⁻⁹ and was maximal among all groups (Â<0.001). In group P 2 the average number of ST in the LFV (15.1±0.31) and the average area of ST ((0.89±0.02) m²×10⁻⁹) were reduced (Â<0.001) relatively to the control group. In group P 3 the average number of ST in the LFV (13.17±0.26) and the average area of ST ((0.52±0.01) m²×10⁻⁹) were reduced (Â<0.001) relatively to the control group. This index was minimal (Â<0.001) among all groups.

In conclusion, fetuses and newborns from mothers whose pregnancy was complicated by pre-eclampsia had considerable changes in the structure of testes and probably can have andrological abnormalities in future.

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Pre-eclampsia, Gestational Hypertension and Intrauterine Growth Restriction (IUGR): comparing perinatal outcomes

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Objective: To compare determinants and perinatal outcomes associated with preeclampsia, gestational hypertension and unexplained intrauterine growth restriction (IUGR).

Method: In a retrospective study, we analyzed 179 pregnancies complicated by IUGR preeclampsia, and gestational hypertension diagnosed in our department, between January 2000 and December 2008. Pregnancies were divided in 3 groups: A- pregnancies complicated by unexplained IUGR; B – pregnancies complicated by IUGR and gestational hypertension; C- pregnancies complicated by IUGR and preeclampsia.

Results: Mean maternal age was similar in the three groups. Uterine and umbilical artery Doppler were anomalous mainly in group C (p<0.001). Gestational age (GA) at delivery was A – 37.4 weeks (w) B – 31.7 w; C – 30.5 w (p<0.001). Prematurity (delivery before GA=37w) was diagnosed in 43.5% in group A, 92.3% in group B and 97.1% in group C (p<0.001). Severe prematurity (before 32 weeks) also was more associated with group C (p<0.001). There were 53.4% C-section in group A vs. 61.5% in group B vs. 91% in group C (p=0.01). The mean birth weight was 2,302g in group A; 1,934g in group B and 1,323g in group C (p<0.001). Newborns from group C (74%) were more often admitted to intensive care unit (p<0.001).

Conclusions: Unlike with unexplained intrauterine growth restriction, the association of preeclampsia is a major risk for severe perinatal morbidity. Gestational hypertension also independently increases perinatal risk when associated to IUGR.

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Pre-eclampsia and HELLP Syndrome complicating multiple gestations: differences considering risk factors and perinatal Results

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Objectives: Comparison of multiple gestations with versus without preeclampsia and HELLP Syndrome complications.


Results: Group 1 represents preeclampsia and HELLP Syndrome complicating multiple pregnancies (7.3%) and group 2 corresponds to multiple gestations without these complications. Comparing group 1 vs. group 2, mean age was 30.0±6.3 [19-41] vs. 30.1±4.6 [18-41] (p=n. s.). Sixty percent vs. 43% were nulliparous (p=0.019) and 10% vs. 21% were pregnancies obtained after assisted reproduction techniques (p=n. s.). Chronic hypertension was diagnosed in 2.3% vs. 1.4% (p=n. s.) and pregnancy-induced hypertension in 8.7% vs. 4.6% (p=n. s.). Gestational diabetes (GD) complicated 8.7% vs. 6.2% (p=n. s.). Monochorionicity was statistically more associated with group 1 (p<0.001). Restriction intrauterine growth was present in 20% vs. 11% (p=n. s.). Gestational age at birth was not significantly different considering both groups. Caesarian section was performed in 80% of gestations from group 1 and 42% from group 2 (p=0.029). Newborns weight did not reach statistical differences. Newborns were admitted in intensive care unit in 22% vs.16% (p=n. s.). Perinatal mortality represented 33‰ in group 1 and 48‰ in group 2 (p=n. s.).

Conclusions: Considering risk factors for preeclampsia and HELLP Syndrome, only nulliparity reached statistical significance. Monochorionicity was statically more associated with development of preeclampsia and HELLP Syndrome. Caesarian section was significantly more frequent in preeclampsia and HELLP syndrome group. Gestational age of newborn, their weight and perinatal mortality were not significantly different.

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Management of severe pre-eclampsia in a district gereral hospital-how good are we?

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Severe pre-eclampsia and eclampsia are relatively rare but serious complications of pregnancy, with around 5/1000 maternities in the UK suffering severe pre-eclampsia. The Confidential Enquiries into Maternal Deaths persistently show substandard care in a significant percentage of the deaths. Every unit therefore has a guideline to standardize the approach to the management of this condition. The aim of our study was to audit our practice with reference to the guideline, over a period of one year. We had 89 patients with hypertension and protienuria in pregnancy. Of these 18 patients had severe pre-eclampsia. Magnesium sulphate was administere for seizure prophylaxis in 61% of cases. Only 72% had appropriate monitoring of vital signs and fluid management. Multidisciplinary management was recorded in all the cases. 41% of patients had caesarean section. The study has highlighted that we are good in appropriate assessment and performing the investigations but should be better in monitoring and documentation. The caesarean rate is higher in this group and the debriefing was inadequate. Severe pre-eclampsia is a condition which if managed appropriately can save a woman’s life. Hence all the staff involved should be aware of the standards of care. We hope that by including management of severe pre-eclampsia as a mandatory component in the annual obstetric emergencies study day in all the units, we will be able to improve our quality of care.

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Objective: Obstetric hypertensive emergencies are life-threatening conditions for both mother and fetus. The most severe complications of eclampsia are that the mother and/or baby die. One from 7 mothers suffers from hypertensive disorder during the pregnancy. The aim of this study is to show incidence of hypertensive disorders and pre-eclampsia, treatment and outcome in 5897 pregnant women in General hospital in Kumanovo in 2006/07/08 year (Department of gyn/obs). Material and methods: History of illness and delivery of 5897 patients treated in General Hospital Kumanovo – Department of gyn/obs during 2006/07/08 year. Results From all these patients 10, 8% suffered from minor or major hypertensive disorders; 13, 1 middle or severe urinary infections; 14, 2 hypoproteinemia; preeclampsia had 2, 01% eclampsia had 7 patients and HELLP syndrome had 5 patients. One mother died. Treatment was by protocol for hypertensive disorders. Outcome: 68% gave birth with C-section versus 12% in other group. Complications in postpartum period had 43, 3% versus 7, 8% in other patients. Low birth-weight babies had 31%. Conclusions: Obstetric hypertensive disorders, eclampsia, and HELLP syndrome are still common and with big rate in our community. Even the mechanisms of disorder are still unknown regular check- up during pregnancy, early treatment in hospital and terminating the delivery in optimal time are very important for mothers and babies life.

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**Hellp syndrome**

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Aim: the investigation and treatment of the pregnant who suffers from preclampsia and is complicated from the HELLP syndrome.

Material-method: The study concerns the treatment of three pregnant women from 31st until the 35th week of gestation that suffers from preclampsia and they are complicated by HELLP syndrome (rapid alleviation of number of platelets-hemolysis, increase of hepatic ferments and ache in epigastrium like cholecystitis ache). In mothers-to-be with HELLP syndrome Caesarean section was done after they had transfused with 6-10 units of platelets aiming at prices before the operation about 50,000/mm³. After the surgery was observed impressive reintroduction of their general condition as well as their laboratorial prices.

Conclusion: The patients that at the duration of gestation are complicated with preclampsia should be checked with regard to their general situation, to the prices of arterial pressure and their laboratorial prices (number of platelets and hepatic ferments) so that they have as much as possible better prognosis.

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Gestational age in pre eclampsia: its correlation with LDL-C and malonyldialdehyde concentrations

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Hypertensive disorders are an important clinical problem in pregnancy and are associated to oxidative stress and lipid alterations. Objectives: To determine associations among gestational age, low density lipoproteins (LDL-C) concentrations and malonyldialdehyde (MDA) in pre eclamptic women. Design: Analytical and longitudinal study of women with pre eclampsia (n=29), superimposed pre eclampsia (n=13) and controls (n=41), with 15 to 40 years of age, in single pregnancies. Setting: University Hospital “Dr. Luis Diaz Soto”. Period: Jan 2007 - Dec 2008. Methods: Blood was withdrawn soon after diagnosis of pre eclampsia and in the controls after 36 Wks. Statistics: Means and standard deviations, Mann-Whitney, Kruskall-Wallis, linear regression and correlation tests. Ethics: Informed consent. Results: 1) LDL-C and MDA concentrations were higher in pre eclamptic than controls (3.85±0.79 vs. 2.71±1.01mMol/L and 0.270±0.130 vs. 0.190±0.04mMol/L x 10 -1 respectively; P<0.05), 2) gestational age was smaller in pre eclamptic women than in controls (37±1 Wks. vs. 40±1.2 Wks., respectively; P<0.05). Conclusions: We find an inverse correlation (p<0.05) among LDL-C concentrations and gestational age in superimposed pre eclampsia (r: -0.642; p<0.05) and among MDA concentrations and gestational age in pe eclamptic women (r: -0.541; p<0.05).

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Can adiponectin predict hypertensive disorder in pregnancy?

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Objective To determine whether adiponectin can predict hypertensive disorder in pregnancy (HDP).

Methods All women with singleton pregnancy and who were at risk of gestational diabetes mellitus (GDM) were studied. They underwent a 50 gram glucose challenge test (GCT) and a blood sample test for adiponectin between 21 and 27 weeks gestation. Subsequently, between 24 and 28 weeks gestation the women underwent a 100 gram oral glucose tolerance test (OGTT). The pregnancy and perinatal outcomes in all women were observed and analyzed.

Results There were 359 women enrolled in this study. Twenty-two cases of HDP (6.1%) and 60 women with GDM (16.7%) were diagnosed. There were no significant difference in age, pre-pregnant BMI, sampling day BMI, weight gain on sampling day and total weight gain during pregnancy in both groups. Serum adiponectin was not significantly lower in HDP than non-HDP women (P =NS). The area under the receiver-operator characteristic curve was 0.5853. In order to predict HDP, an arbitrarily cut-off value of adiponectin was determined. With the adiponectin cut-off value <4.4 µg/ml, the sensitivity, specificity, PPV and NPV were 4.55%, 90.50%, 4.76% and 93.14% respectively. At this cut-off value, only 1 out of 22 cases of HDP could be identified.

Conclusion The levels of adiponectin in women with HDP were not significantly different from those without HDP and could not predict HDP.

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Troponin I and homocysteine levels in mild and severe preeclampsia

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Objective: To investigate troponin I and homocysteine in pregnant women with severe and mild preeclampsia.

Methods: 43 women with mild and 22 women with severe preeclampsia and 34 healty pregnant women included. Homocysteine and troponin levels of three groups were measured at admission and compared.

Results: Mean troponin I levels were 0.005ng/ml, 0.0116ng/ml and 0.007ng/ml in healty pregnant women and mild and severe preeclampsia respectively, these Results were similar among three groups (p=0.276). Homocysteine levels were similar in mild and severe preeclampsia groups and significantly higher than healthy pregnant women.

Conclusions: Troponin I levels are not significantly increased in both mild and severe preeclampsia. Homocysteine increases in preeclampsia, but severity of preeclampsia is not correlated with homocysteine levels.

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Plasminogen activator inhibitor type 1 and fibronectin in early prediction of preeclampsia

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Background: Preeclampsia has been shown to be linked with the endothelial damage and abnormal activation of the coagulation system. Our aim was to evaluate a role of plasminogen activator inhibitor type 1 (PAI-1) and fibronectin in the early prediction of disease.

Materials and methods: The prospective case-control study was conducted in total of 100 pregnant women. 18 of these were later diagnosed with preeclampsia (>32 weeks) and 82 normal pregnancies served for controls. Plasma levels of PAI-1 and fibronectin (ELISA assay) were determined 3 times during each pregnancy at 8-10 weeks, 15-17 weeks and 25-27 weeks. All data were statistically analyzed using Student t-test.

Results: PAI-1 plasma levels at 8-10 weeks were 35.2±23.3ng/mL in women with preeclampsia compared to 35.6±22.0ng/mL of the healthy controls (p=0.952). At 15-17 weeks the corresponding values were 78.0±11.7ng/mL and 51.7±16.9ng/mL (p=0.222), and finally, at 25-27 weeks, 117.0±26.1ng/mL and 73.1±26.7 (p=0.0006). Circulating plasma fibronectin levels at 8-10 weeks were 348.2±79.5mg/mL in preeclampsia and 352.9±120.0mg/mL in controls (p=0.91). At 15-17 weeks the values were 269.3±43.0mg/mL and 329.4±110.0mg/mL in controls (p=0.284), and finally, at 25-27 weeks, 442.0±104.0mg/mL and 349.3±113.1mg/mL (p=0.0034).

Conclusions: Relatively late rise of PAI-1 and fibronectin as biomarkers of endothelial damage makes them better diagnostic and prognostic factors for onset of preeclampsia after 32 weeks than valuable predictive markers of disease development in the early pregnancy.

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PIH and nucleotides

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Aim is to analyze nucleotides (AMP, IMP, GMP, ADP, GDP, UTP, ATP, GTP) in erythrocytes in pregnant women with PIH as well as the presence of urine acid in the serum and urine.

Methods: Determination of nucleotides, using spectrophotometric method according to Kohn was applied. Results: The investigation included 40 pregnant women with PIH and 40 women with normal pregnancy (control group). The values of adenosine diphosphate (ADP) were also increased in erythrocytes of pregnant women with PIH 83.632 nM in relation to the women with normal pregnancy (82.195nM), same as, of guanosin diphosphate (GDP) 9.127nM (PIH): 7.647nM in the control group, then uridin triphosphate (UTP) 4.089nM (PIH) in relation to healthy pregnant women - 3.976nM and adenosine triphosphate (ATP) 102.157nM (PIH): 99.199nM in the control group. Value of guanosin monophosphate (GMP) was slightly lower in pregnant women with PIH of 3.09nM in relation to the control group - 5.96nM, as well as guanosin triphosphate (GTP) 8.110nM (PIH) in relation to the value of healthy pregnant women of 8.945nM. The concentration of urine acid in serum of pregnant women with PIH was increased and it was 201.0nM in relation to the control group of 180.0nM.

Conclusion: Our Results indicate that disorders of nucleotide metabolism are evident in pregnant women with PIH, associated with increased secretion of urine acid. The activity of Na, K and Mg ATP has been estimated in erythrocytes of PIH patients, and the decreased ATP activity was recorded.

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Expression profile of inflammatory markers in hypertensive diseases of pregnancy

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Objectives: Evaluation of inflammatory markers associated with pregnancies complicated by gestational hypertension, preeclampsia and HELLP Syndrome

Material and Methods: Study of 200 pregnancies complicated by gestational hypertension, preeclampsia and HELLP Syndrome. C-reactive protein (CRP), D-dimer and fibrinogen were analyzed in each group at the admission.

Results: Pregnancies complicated by gestational hypertension (n=79), had mean CRP 1.80 [0.05-0.30], D-dimer 2.47 [0.09-59.15] and fibrinogen 4.54 [1.06-6.00]. In preeclampsia patients (n=93), mean CRP was 1.54 [0.30-5.80], D-dimer 2.82 [0.60-22.70] and fibrinogen 4.42 [1.44-6.84]. In HELLP Syndrome (n=28), mean CRP was 3.20 [0.05-8.39], D-dimer 8.40 [0.6-38.2] and fibrinogen 4.15 [1.02-5.60]. CRP (p=0.041) and D-dimer (p<0.001) value were statistically associated with HELLP Syndrome. CRP (0.011) and D-dimer (p<0.001) were higher in preeclampsia than gestational hypertension. In preeclampsia and HELLP Syndrome patients, were not described significant differences. CRP (p=0.003) and also D-dimer (p<0.001) were significantly higher in HELLP Syndrome than in gestational hypertensions.

Considering preeclampsia and preeclampsia developing HELLP Syndrome, D-dimer (p=0.005) was the only marker significantly associated with the last group. On the other hand, in gestational hypertension patients and gestational hypertension complicated by preeclampsia, fibrinogen (0.007) value was significantly associated with the last group.

Conclusions: CRP and D-dimer was significantly higher in HELLP Syndrome than remaining hypertensive diseases. Preeclampsia and HELLP Syndrome patients had higher CRP and D-dimer than gestational hypertension. D-dimer value was associated with development of HELLP Syndrome in preeclampsia patients. Fibrinogen was associated with development of preeclampsia in gestational hypertensive patients.

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Maternal serum levels of androgens in normal and hypertensive pregnancies - 
the potential benefit of longitudinal testing

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Objective: Alterations of the steroid hormone profiles have been suggested to be involved in the 
pathophysiology of pregnancy-induced hypertension (PIH). As previous findings often are discussed 
controversially, aim of our study was to evaluate the benefit of longitudinal testing of maternal serum 
concentrations of androgens in pregnancies with PIH.

Methods: Serum levels of testosterone, dihydrotestosterone, androstenedione and 
dehydroepiandrosteredione-sulfate were measured in 40 nulliparous women with PIH and 40 
normotensive pregnant women, matched for gestational age, determined by enzyme linked 
imunosorbent assay.

Results: Compared to controls, the median serum levels of androstenedione (A) and testosterone (T) 
were significantly elevated in women with PIH. (A 6.3 and 5.0ng/ml; T 1.8 and 1.1ng/ml; p=0.005 and 
p=0.04). The difference between the median serum levels of dihydrotestosterone and 
dehydroepiandrosteredione-sulfate in pregnant women with pregnancy-induced hypertension and 
controls was not significant.

Conclusion: Women with PIH have elevated serum levels of androstenedione and testosterone. To 
evaluate the prognostic value of maternal serum concentrations of those steroid hormons, 
longitudinal testing in normal and complicated pregnancies is essential. For that, a retrospective pilot 
study investigating serum levels of androstenedione and testosterone in pregnancies before and after 
diagnosis of SIH and in matched control-pregnancies was designed and initiated.

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Serum concentration of placenta growth factor (PLGF) and endothelial growth factor receptor (VEGFR1) in pregnant women with preeclampsia - preliminary report

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Introduction: The etiopathogenesis of preeclampsia is not fully explained but it is associated with an incorrect implantation of the trophoblast, insufficient relaxation of spiral arteries and disturbed blood flow within placenta. These disturbances may effect endothelial cells and therefore a concentration of angiogenic factors and their receptors.

Aim of the study: An assessment of serum PlGF and VEGFR1 level in pregnant women with preeclampsia.

Materials and methods: The study comprised 37 preeclamptic women aged 29.6±4.9 years and 22 healthy gravidas aged 26.6±3.2 years who served as a control group. Serum PlGF and VEGFR1 was measured in third trimester of pregnancy, in the study group between the 29th and 40th - and in the control group between 26th and 36th week of gestation. Both parameters were measured by ELISA commercial KIT.

Results: Median values of serum PLGF level in preeclamptic women were significantly lower then in controls: 166.0 pg/ml (range 31.3-867.6 pg/ml) vs. 528.1 pg/ml (range 86.5-1146.5 pg/ml), respectively. Conversely, median values of serum VEGFR1 level in preeclamptic women were significantly higher then in controls: 691.8 pg/ml (range 53.2-3225.9 pg/ml) vs. 246 pg/ml (range 72.7-2679 pg/ml), respectively.

Conclusions: The serum PlGF concentration is clearly decreased whereas the concentration of the soluble form of VEGFR1 is increased in women with preeclampsia. Thus both parameters seems to be useful as a markers of preeclampsia.

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Angiogenic growth factors in maternal and fetal blood in pregnancies complicated by preeclampsia - preliminary report

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Introduction: The role of angiogenic disturbances in preeclampsia is still a matter of debate. Therefore we evaluated serum levels of different angiogenic factors (PLGF, VEGF, VEGFR1 and VCAM) in maternal and fetal sera.

Materials and methods: The study group comprised 16 women with preeclampsia and their offspring whereas twelve normotensive pregnant women and their offspring served as controls. At delivery, maternal and fetal umbilical blood was sampled and angiogenic factors were subsequently measured by enzyme linked immunosorbent assay (ELISA).

Results: In comparison to controls, preeclamptic women showed significantly lower serum concentrations of PLGF and significantly higher serum VEGFR1 and VCAM levels. The same tendency was found in fetal sera. In most cases, the maternal serum VEGF concentrations were undetectable. In contrast, fetal serum VEGF concentrations were detectable but any significant differences between fetuses of preeclamptic group and controls were found.

Conclusions: Our Results indicate that angiogenic factors contribute to the pathogenesis of preeclampsia. Further studies are necessary to assess their clinical usefulness as markers of preeclampsia.

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**Endocrine gland – derived vascular endothelial growth factor in aetiology of pre-eclampsia – our experiences**

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Background: Pre-eclampsia (PET) is a hypertensive complication of 7-10% of all pregnancies worldwide. Endocrine gland-derived vascular endothelial growth factor (EG-VEGF, prokineticin 1 - PK-1) and its receptor (PKR1) has been identified. The main function of EG-VEGF is angiogenesis, and therefore it may play a crucial role in impaired endothelial functioning in pre-eclamptic pregnancies.

Materials and Methods: We designed two study groups: pregnant PET patients and healthy controls. The samples were obtained during the elective caesarean sections of the consented patients. We have collected myometrial and placental biopsies from 40 patients (19 were PET patients). Tissue was collected and fixed or frozen. RNA was extracted and subjected to quantitative PCR and fixed tissue was used for immunohistochemistry. A sample of every tissue was cultured in vitro, following stimulation with EG-VEGF and the activation of the intracellular pathways was assessed.

Results: There is a peak response in 30 minutes after adding ligand (EG-VEGF) to the pre-incubated tissue. This pattern is alike in myometrium and placenta of the controls whereas the PET have the response in the placenta blurred. The response to the ligand is stronger in placentas of the controls than in their myometriums whereas in PET it is completely opposite. In immunohistochemistry slides greater presence of PK1 and PKR1 was seen in endothelial cells of the normals. RT-PCR shows greater expression of the PKR in myometriums then in placentas.

Conclusions: From this stage of our research we can conclude that signalling and expression of EG-VEGF in PET patients are disturbed.

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Homocysteine in pregnant women with moderate to severe preeclampsia

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The aim of the study was to assess possible variations in homocysteine level according to the severity of preeclampsia, maternal age, body mass index (BMI) and body weight, and possible association of maternal and neonatal homocysteine levels. The study included 70 pregnant women with preeclampsia divided according to study parameters, and 70 umbilical blood samples. The level of homocysteine was statistically significantly higher in women with severe preeclampsia as compared with those with moderate preeclampsia (8.813±1.433 vs. 5.248±0.984 µmol/L; p=0.000). Positive correlation was found between neonatal and maternal homocysteine (r=0.72; p=0.000). There was no statistically significant difference in homocysteine level between women aged >35 and <35 (7.250±2.737 vs. 6.239±1.771 µmol/L; p=0.151); between women reporting weight gain <15 and >15kg (6.313±2.427 vs. 6.603±1.690 µmol/L; p=0.162); between women with body weight <90 and >90kg (6.559±1.906 vs. 6.262±2.404 µmol/L; p=0.302); and between women with BMI <25 and >25 (6.264±1.713 vs. 6.297±2.396 µmol/L; p=0.199). Accordingly, severe preeclampsia was associated with higher homocysteine levels than moderate preeclampsia. The levels of homocysteine recorded in women with preeclampsia influenced the levels of homocysteine in their newborns. Based on the study results, maternal age, pregestational BMI, weight gain and body weight had no effect on homocysteine level in pregnant women with preeclampsia.

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Expectant management of severe pre-eclampsia

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Objective: Describe the cases of pregnant women with severe pre-eclampsia below 32 weeks of gestation, who were managed conservatively.

Methods: Retrospective study including seven women with severe pre-eclampsia who were treated with expectant management between October 2007 and January 2009.

Results: Five of the seven cases were nulliparous women, the mean age was 32 (23-40) years old, the mean gestational age at diagnosis was 29 (range 25 -32) weeks. They received treatment with magnesium sulphate and labetalol in continuous intravenous infusion, steroids for fetal lung maturation and close maternal and fetal surveillance. The mean prolongation of gestation was 11 (6-18) days. Delivery route was vaginal in 3 patients (43%) and the rest underwent caesarean section (57%). The indications for delivery were: onset of labor, Hellp Syndrome, two cases with deterioration in maternal respiratory function, one of them labelled as acute pulmonary edema, suspected chorioamnionitis, gestational age of 34 weeks and a evidence of deterioration of fetal well-being. Five newborns admitted to neonatal care unit for low birth weight, without other pathology except respiratory distress in one case. 85% of patients had an altered uterine artery Doppler

Conclusion: Expectant management of severe pre-eclampsia makes possible to prolong gestation and to improve perinatal outcome without increasing maternal morbidity. It should be performed only in a select group of patients, with a close maternal and fetal surveillance and in hospitals with adequate maternal and neonatal intensive care unit.

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Ophthalmic artery resistive index in preeclampsia: Differential diagnosis

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Background: Preeclampsia is the main condition in the clinical spectrum of hypertension in pregnancy. Although its diagnostic criteria have been standardized since the Working Group Report of High Blood Pressure in Pregnancy (2000), preeclampsia diagnosis remains a subject of debate. The purpose of this study was to verify OARI accuracy in preeclampsia differential diagnosis.

Methods:: Women admitted with high blood pressure (BP ≥140/90mmHg) were included in this study. Classification in isolated preeclampsia (IPE), superimposed preeclampsia (SPE), chronic hypertension (CH) and transient gestational hypertension (GTH) was performed according to the Working Group Report of High Blood Pressure in Pregnancy (2000). OARI was obtained at admission with orbital color Doppler ultrasonography. OARI accuracy in preeclampsia diagnosis was evaluated by the area under ROC curve. The finest cutoff point for preeclampsia diagnosis was established.

Results: One hundred seventy-two women with preeclampsia (IPE and SPE) and 186 women without preeclampsia (CH and TGH) participated in this study. Among women with preeclampsia, 32 received preliminary diagnoses of CH (19) and TGH (13) after the first non significant 24 hour proteinuria. Eighty-three women with preeclampsia fulfilled criteria of severe disease. Women with preeclampsia presented significant lower OARI compared with women without preeclampsia (0.57±0.05 and 0.72±0.06, p<0.0001). The area under ROC curve was 0.921±0.011 (p<0.0001). The cutoff point of 0.65 OARI provided 0.92 sensitivity and 0.87 specificity in preeclampsia diagnosis.

Conclusions: Data support OARI as an accurate preeclampsia biomarker. OARI lower than 0.65 at admission suggests preeclampsia.

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**Ophthalmic artery resistive index in preeclampsia: Identification of severe disease**

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**Background:**
Due to its unpredictable clinical course, preeclampsia management remains challenging. Therefore, the search for additional markers of severity is necessary desirable to increase maternal and fetal safety in preeclampsia.

**Methods.**
Women admitted with high blood pressure (BP ≥140/90mmHg) and ≥0.3g per 24 hour proteinuria were included in this study. Classification as mild and severe preeclampsia was performed according to the Working Group Report of High Blood Pressure in Pregnancy (2000). OARI at admission was obtained with orbital color Doppler ultrasonography. OARI accuracy in severe preeclampsia identification was obtained with the area under ROC curve. The finest cutoff point was established.

**Results:**
One hundred seventy-two women with mild preeclampsia and 196 women with severe preeclampsia participated in this study. Among women with severe preeclampsia, 36 received the preliminary diagnosis of mild preeclampsia and fulfilled criteria of severe disease during hospitalization. Women with severe preeclampsia presented significant lower OARI compared with women with mild preeclampsia (0.53±0.02 and 0.58±0.04, p<0.0001). The area under ROC curve of 0.786±0.028 for severe preeclampsia diagnosis. The cutoff point of 0.58 OARI provided 0.82 sensitivity and 0.79 for severe preeclampsia diagnosis. Among women diagnosed with mild preeclampsia who later fulfill criteria of severe disease, 32 (88%) presented OARI<0.58 at admission.

**Conclusions:**
Data support OARI as an accurate biomarker of severe preeclampsia. OARI lower than 0.58 at admission suggests severe preeclampsia as well as high risk of progression to severe preeclampsia.

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The role of maternal angiogenic factors and uterine artery Doppler to predict preeclampsia in the second trimester of pregnancy

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Objective: Investigate the utility of sFlt-1 and uterine artery Doppler as useful markers of preeclampsia prediction during second trimester of pregnancy.

Methods: 72 pregnant women, who presented epidemiological risk factors to preeclampsia (PE), were followed until delivery in a cohort study. Preeclampsia was defined according to NHBPEP, 2000 criteria. Receiver-operating characteristics curves (ROC) were used to determine maternal plasma concentrations of PlGF, sFlt-1 and sFlt-1/PlGF ratio accuracy to predict PE. Cutoff points for angiogenic factors were calculated using sensitivity values of 100%, 90% and 80% and then associated to bilateral notching uterine artery Doppler, in order to select the best predictors.

Results: PE was present in 15.3% of the patients. Through the analysis of ROC curve, angiogenic factors levels at second trimester were found to be optimal predictors of preeclampsia. Area under the curve was 0.94 (0.89 to 0.99, 95% CI), 0.88 (0.57 to 0.85, 95% CI) and 0.95 (0.87 to 1.0, 95% CI) for PlGF, sFlt-1 and sFlt-1/PlGF ratio, respectively. At 90% sensitivity for the biomarkers (743.5pg/ml for sFlt-1, 159.5pg/ml for PlGF and 6.6 for sFlt-1/PlGF ratio) higher likelihood ratio and relative risk were observed, comparing to 80% and 100% sensitivity. The association between bilateral notch and 90% sensitivity PlGF or sFlt-1/PlGF ratio cutoffs did not improve diagnosis accuracy to predict PE, although all associations were good predictors.

Conclusion: Maternal plasma PlGF, at second trimester, seems to be an effective marker of PE prediction in high risk groups, but do not improve when associated to bilateral notching.

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Changes in the maternal hepatic blood flow in pregnant women with preeclampsia

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Preeclampsia is a polymorphic disorder which includes vascular changes in maternal cerebral, hepatic and renal blood flow that may cause serious maternal pathology. The aim of this study was to investigate if there are changes in maternal hepatic blood flow in preeclamptic women compared to normotensive pregnant women and to evaluate those changes after delivery.

Methodology We evaluated maternal hepatic blood flow by measuring Doppler blood flow in common hepatic artery (CHA) and portal vein (PV). Doppler parameters were: Pi and Ri in CHA, mean velocity in PV and liver vascular index (PV MV/CHA PI). The measurements were done in 100 women with mild preeclampsia, 101 women with severe preeclampsia and 100 normotensive pregnant women.

Results: We found increased hepatic artery pulsatile and resistance indices in women with preeclampsia compared to normotensive women, especially in severe preeclampsia and HELLP syndrome. There were no significant differences in portal vein blood flow and liver vascular index. After delivery those indices are still higher in preeclamptic women, but decreased comparing to pregnancy.

Conclusion: Elevated Doppler indices in only hepatic artery blood flow in women with preeclampsia suggest that arterial vasoconstriction is present in preeclampsia and implies that those changes may cause severe complications.

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Preeclampsia - Does prepregnancy body mass index predicts the perinatal outcome?

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Background: Maternal obesity is an important risk factor for preeclampsia. However, in women who have already developed preeclampsia, the effect of their weight in the disease severity is still unclear. The aim of this study is to detect if maternal BMI predicts the perinatal outcome.

Material and methods: We analyzed 115 preeclamptic women who received medical assistance at our institution, between January 2005 and June 2008. These were divided in 3 groups: (A) BMI<25kg/m², (B) 25kg/m²≤BMI≤29.9kg/m², (C) BMI≥30kg/m². Maternal characteristics, obstetric histories and neonatal outcomes were compared.

Results: The 115 women were distributed to groups A (53), B (28) and C (34). Average maternal age was 30.4 (A), 30.5 (B), and 29.6 (C) years (p=n. s.). In all groups, the majority of the patients were nulliparous (A-58.5%, B-57.1%, C-58.8%). Six multiple pregnancies occur: 4 in group A and 2 in group B (p=n. s.). Average gestational age at hospital admission was 33.6(A), 34.2(B), and 34.8 (C) weeks (p=n. s.). Prophylactic MgSO4 was used 20.5% (A), 7.1% (B), and 11.8% (C) (p=n. s.). Labor was induced 13.2%(A), 21.4%(B), and 41.1%(C) (p=0.011) and occurred, in average, at 34.1 (A), 34.7(B), 35.1(C) weeks (p=n. s.), with caesarean rates of 88.7% (A), 67.9% (B), 73.5% (C) (p=n. s.). Neonate birth-weight was 2048 (A), 2248 (B), 2356 (C) grams (p=n. s.). In group C there were three stillbirths and one neonatal death (p=0.026). Statistically, maternal complications (A-30.2%, B-17.9%, C-11.8%) and neonatal morbidity (A-22.6%, B-25%, C-9%) do not differ in the 3 groups.

Conclusions: The risk of preeclampsia rises with increasing prepregnancy BMI. Nevertheless, despite a great number of stillbirths and neonatal deaths, in our population obese preeclamptic women had no worse perinatal outcomes.

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Nephrotic syndrome reagent to pneumonia vs. severe preeclampsia

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Discussion: the case shows the big variety of clinical entities that can pose of differential diagnostic during the pregnancy, in a patient with pharmacopeia reduced by the gestation and by his drugs allergies.

Primipara of 31 years, at 31 weeks ingress under suspicion of atypical pneumonia. Antecedents: sinusitis, allergic rhinitis and allergy to penicillin.

Current gestation: without incidents. Chronology of problems:

1.- Atypical pneumonia. From the 29 weeks: fever, productive cough and diarrhea. She initiates Erythromycin. To the sixth day, get worse with dysphonia. Radiography showed discreet increase of pulmonary density and leucocytosis. Urine sediment: 100mg/dl proteins. Blood culture was negative. Legionella antigen in urine, PPD and spittle culture were negatives. Antibodies for Mycoplasma Pneumoniae were positive: 1/160

To realize fetal maturation and initiates Rifampin 600mg/24h ev.

2.- Suspicion of severe preeclampsia: she presents edemas in inferior extremities and TA limit. Urine protein 24 hours: 2064mg.

It realizes hydric balance, analytical control and of TA.

3.- Following week of antibiotic to appear severe elevation of ALT and AST. It considers that the hepatic affectation does not depend of the preeclampsia and recalls the Rifampin which it’s stopped. To the 3 days, improves the hepatic function. Evolution: it improves the respiratory picture and protein urine too: Nephrotic syndrome reagent to the pneumonia.

Hepatic toxicity secondary to rifampin improves when it's stoped.

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Eklampsia in the third trimester of pregnancy and systemic lypys erythematous a case report

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Aim: We here describe one rare case of eclampsia and SLE who diagnosed, evaluated and successfully managed recently in our department.

Material-Methods: A 31 year old woman gravida 1, para 0 in her 25w of pregnancy arrived in obstetric gynecology clinic of general hospital of Pyrgos Greece in status epileptikus. Patient with personal History of: SLE, Hypothyroidism (Thyroiditis Hashimoto), pericarditis. B Level ultrasonographic examination was performed in a private center in 23 weeks and 6 days of gestation has sown 21week and 6 days gestational age by us. In during of eclamptic seizures blood pressure (BP) was 175/110mmHg. Laboratory Findings: HB 12.0g/dl, HCT 36.3%, PLT 251 K/UL WBC 15.700 NEUT 85.0% LYMPH 12.4% MXD 2.6%, Uric acid level 8.9mg/dl, albumine 2.9g/dl, Tproteine 3.80, calcium total 8.2mg/dl, LDH 325mg/dl, CK 152 IU/L, CKMB 43 IU/L, ALF 106 IU/L, γGT 26 IU/L, SGOT (AST) 49 IU/L, SGPT (ALT) 47 IU/L, CRP 4.1mg/dl, k 4.8mmol/L, 136 Na mmol/L, amylase 79 IU/L, ptSEC 11.6, INR 0.96, Appt 34.1, D-dimer 1909.92ng/dl, Gly 85mg/dl, urea 39mg/dl, creatinine1.2mg/dl.

Results: padded tongue depressor. were given intravenous dextrose 5% 1000cc with 4 ampMgS4.2 amp epanutin in 100cc NaCl 0.5%, im 1 amp nadroparine calcium 0.6ml (5700IU anti-xa) 0.5% immediate incubation and delivery by caesarean section. Women and newborn were transported to institutions of tertiary care where better obstetrical and neonatal care.

Conclusion: Pregnant women with SLE have an increased risk of Eclampsia, Proeclampsia.

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Posterior reversible encephalopathy syndrome in a triploid pregnancy complicated by HELLP Syndrome

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Pre-eclampsia still remains an important cause of maternal and perinatal morbidity and mortality. It is a pregnancy-specific multi-system disorder with unpredictable, variable and widespread manifestations.

Early-onset pre-eclampsia and/or eclampsia (16-24 weeks) are rare. When it occurs, it is frequently associated with fetal and placental anomalies. Hydatidiform moles, fetoplacental triploidy with partial molar changes and idiopathic hydrops fetalis have been the commonly reported associations. In such cases it has been postulated that the increase in paternal genetic material associated with the triploid diandric placenta may support the role of immunologic factors in the development of pre-eclampsia.

We report an unusual case presenting at 16 weeks of gestation, with uncontrollable hypertension and proteinuria that progressed to severe HELLP syndrome. She developed focal neurological deficits post partum. This presents a wide range of diagnostic possibilities. Various differential neurological diagnoses in this case were considered including haemorrhage, infarction, vasculitis, pontine or extrapontine myelinolysis and posterior reversible encephalopathy syndrome (PRES). After imaging and further investigations it became apparent that this was a case of PRES, a rare sequelae of pre-eclampsia and not previously reported in the context of triploidy. The patient: She recovered fully nearly three months postpartum.

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Temporary blidness in hyperemesis gravidarum

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Hyperemesis gravidarum is a severe and disabling condition with potentially life threatening complications. We report the case of 30 year old woman who presented with hyperemesis gravidarum during the first trimester of twin pregnancy. A transient blidness during 48 hours was observed and woman suffered from ataxia. correction of dehydration and electrolyte disturbance added to intravenous thiamine administration with prednisolone provided rapid improvement and complete recovery. For severe, prolonged hyperemesis, consideration should be given to intravenous thiamine supplementation to prevent Wernicke encephalopathy.

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Addisons disease in a patient pregnant with monochorionic twins

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Introduction: Addisons disease is combined with a deficiency of cortisol and aldosterone. In women, the autoimmune form is more common and associated in up to 40% with other autoimmune conditions. Prior to the advent of steroid therapy it was associated with a high maternal mortality. Adrenal antibodies cross the placenta but neonatal adrenal insufficiency is rarely encountered.

Case report: We report on a mother who had a spontaneous monochorionic diamniotic (MCDA) twin pregnancy and Addison's disease. Morbus Addison had been diagnosed at the age of 19 years due to clinical symptoms of hypotonia, nausea, fatigue and hyperpigmentation. The patient received 25mg hydrocortison and 0.2mg 9-alpha-fluorhydrocortison/day and got pregnant of MCDA twins. Hydrocortison was increased to 50mg/day considering the increased plasma volume in multiple pregnancy and clinical symptoms of nausea. The pregnancy was uneventful until 31 weeks when she was admitted with PPROM. The patient received oxytocin-antagonists and betamethasone. Due to progression of labor she received peridural anaesthesia and parental application of 100mg hydrocortison/6hours. With fully dilatation and both twins in vertex position the first twin developed variable decelerations and a Cesarean section was performed. Both boys had a normal outcome and did not need steroid supplementation nor ventilation. The mother presented with hypotension and diuresis postnataally but recovered rapidly.

Conclusions: When interpreting Results of cortisol in pregnancy one should consider that total serum and free cortisol levels are increased and an abnormally low cortisol level may fall within the normal non-pregnant range.

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The frequency rate and obstetric outcome in phenylketonuria pregnancies. Our experience

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Aim: The maternal phenylketonuria syndrome is caused by high blood phenylalanine concentrations during pregnancy and presents with serious fetal anomalies, especially microcephaly, congenital heart disease and mental retardation. The purpose of this study was to evaluate the pregnancy outcome associated with phenylketonuria (PKU).

Method: In a retrospective study between 1990 and 2007 in our Department, we reviewed four cases of phenylketonuria-pregnancies, with an average maternal age of 27.5 years. Pregnancy complications such as preeclampsia, low birth weight, type of delivery and inta-and postpartum complications were studied.

Results: In one case a 33 year old woman had been diagnosed as having PKU only after a pregnancy with maternal PKU embryopathy, in order to emphasize that undiagnosed maternal phenylketonuria still exists. This fetus was dead during the labor. In the other three cases maternal PKU syndrome were diagnosed by prenatal screening. During pregnancy we determined the Phe blood levels weekly and these levels were concomitant with the currently recommended Phe concentration (120-360µmol/l). The pregnant women underwent in a suitable diet plan. The ultrasound recordings in the first and second trimester showed no anatomical anomalies and finally a normal child without dysmorphic features was born. One woman gave birth with normal term- labor and 2 had a Caesarian section with premature labor. The children were born without dysmorphic features

Conclusion: The prevention of the PKU pregnancy by use of effective programs of diet would decrease and eliminate the pregnancy complications.

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Influence of thyroid disorders on pregnancy outcome

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Introduction: Thyroid disease is present in 2-5 percent of women and it is common in pregnancy. Several of the thyroid disorders which tend to occur during pregnancy are autoimmune in nature. Abnormal levels of the thyroid hormones and thyroid antibodies can influence the course and outcome of pregnancy. The aim of the study was to evaluate the influence of the thyroid disorders on pregnancy outcome.

Material and Methods: We examined 93 patients, who underwent Caesarean section in Institute for Gynecology and Obstetrics, Clinical Center of Serbia. We evaluated pregnancy outcome and condition at neonatal birth. Hyperthyroidism was diagnosed in 21% of the patients, the rest had hypothyroidism. Control group consisted of randomized patients who underwent Caesarean delivery, without thyroid disorders.

Results: Incidence of preterm delivery was 15%, without statistical difference in relation to the control group (p>0.05). Caesarean delivery was urgent in 31% of cases, without the statistical difference to the control (p>0.05). Thyroid disorders were adequately treated in 69% of patients. Diabetes mellitus occurred in 22%, hypertension in 25%, and the autoimmune diseases in 32% of the patients. Fetal asphyxia occurred in 12% of the cases and 5.8% babies had low birth weight. Morphometric parameters were not different in relation to the control (p>0.05). Most of the babies were born in term (p<0.01), most of them without fetal macrosomia (p<0.01), most without asphyxia (p<0.01).

Conclusion: Early detection and treatment of thyroid disorders significantly can reduce the known pregnancy-complication and improve neonatal morphometric parameters in patients with thyroid disorders.

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The outcomes of pregnancy and neonatal in women with subclinical hyperthyroidism

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In reproductive ages, thyroid disorders are the second most common endocrine disorder after diabetes. The treatment of thyroid disorders during pregnancy are important to prevent adverse maternal and fetal outcomes.

Subclinical hyperthyroidism is characterized by a serum TSH concentration below the lower limit of reference range, but free T4 and free T3 concentrations within normal reference range. In general population, the incidence of subclinical hyperthyroidism is 0.6-16% and 1.7% in pregnant women (1-2-3). Even though the negative effect of subclinical hyperthyroidism on the neonatal and pregnancy outcomes has not yet shown, the subject has not been studied in detail.

The aim of our study is demonstrate prevalence and impact of subclinical hyperthyroidism in pregnant women.

Materials and Methods: This is a retrospective study and include 1263 pregnant who presented for prenatal care and were screened serum TSH at The our Department of Obstetrics and Gynecology between 2003 and 2007. We evaluated age, gestational age, parity, adverse consequences of pregnancy and neonatal outcomes in women of subclinical hyperthyroidism. Statistical analysis was performed by using SPSS. A p value of <0.05 was considered as statistically significant.

Results: 92 of 1263 pregnant women had subclinical hyperthyroidism. Subclinical hyperthyroidism was appeared more common in women between 25 and 35 ages and parous women. Respectively, the incidence of preeclampsia, diabetes, intrauterine growth restriction, placental abruption, caesarean and malpresentation in women with subclinical hyperthyroidi are %2.17, %2.17, %1.08, %1.08, %65.2 and %3.2 (Table1). Neonatal outcomes were also evaluated; we found major malformations 3.2%, chromosomal abnormalities %1.08, neonatal hypothyroidism %1.08, neonatal convulsion %1.08, decreased the apgar score %5.4, Respirator distress syndrome %1.08 in women with subclinical hyperthyroidism (Table2). There were no statistically significant changes the consequences of pregnancy and neonatal of women with subclinical hyperthyroidism when compared with women of normal thyroid screening.

Discussion: Early diagnosis and treatment of thyroid disease during pregnancy is important in preventing adverse maternal and fetal outcomes. The impact of suclinical hyperthyroidism on the consequences of pregnancy and neonatal is controversial issue. Subclinical hyperthyroidism in pregnancy has not been found to be associated with adverse outcomes and also, there is insufficient evidence to show requirement of treatment of pregnant women with subclinical hyperthyroidism. In our study, the incidence of subclinical hyperthyroidism was found 7.2% and none of pregnant women with subclinical hyperthyroidism were treated. According to our Results, subclinical hyperthyroidism was not associated with adverse outcomes in pregnant women. But, studies are required to ascertain the long-term fetal effects of maternal subclinical hyperthyroidism.

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Does emperor need a new clothe? Knowledge of the population of Juzna Backa district about iodine importance for human health

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Iodine deficiency disorders (IDD) represent a great public health problem due the long-term health consequences. Iodine deficiency is the single most common cause of preventable brain damage worldwide today; the more common effect is a reduction in learning capacity leading which lowering socioeconomic development of whole population. Universal salt iodization has been accepted as the most appropriate way to eliminate IDD.

Aim of the study: consider population knowledge about importance of iodine for human health.

Methods and materials: survey conducted in 2005, among adult population in Juzna-Backa district showed embarrassing lack of knowledge about health effects of iodine deficiency (43% didn't know neither negative health consequences, nor importance of iodine on growth, brain development and general health; 53.7% knew that goiter is a consequence of insufficient iodine intake; 7.3% were aware that lack of iodine causes cretinism). After three years of promoting importance of iodine for human health (media, brochures, lectures etc.), the same population was interviewed again about it. Results showed significant improvement: more than 90% know that iodine is important for normal brain development and mental functions: for over 73, 4% the main informational source were audio-visual media; about 20% got information from neighbors, cousins and friends; only 30% heard about it from medical professionals.

Conclusions: media plays a significant role in forming public awareness about important health issues. Constant spreading of medical information is needed not only for new, but also for existing facts relevant for health.

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Analysis of maternal deaths (Lower Saxony 2002 - 2007): lesson learned: A surveillance-system

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Background:
Maternal mortality and rare disorders in pregnancy are unusual but tragic events in Germany (like in most European Countries). Until now maternal deaths only were analyzed basically in the mandatory perinatal quality assurance program (PQP). Nevertheless it’s necessary to get deeper view and knowledge about incidents, risk factors and prevention of “emergency” care.

Methods:
In the federal state of Lower Saxony 19 cases of maternal deaths (2002 – 2007) were investigated by a confidential enquiry. Firstly the regarding data set of the PQP and secondly an additional structured data sheet were analyzed by a group of experts (obstetricians, midwives…). Finally every single case of the maternal deaths was discussed between the experts and obstetricians in the concerned hospitals.

Results:
Dialogue by experts increases information about:
- cause of death (+100%),
- hospital admission, clinical process of birth (+70%) and
- process in pregnancy (+30%).

Reliable classification of maternal deaths only was possible by the three-step approach. First information was obtained about maternal risk factors (e. g. higher age of pregnant women, obese), alternative strategies of treatment in difficult situations and for “normal” deliveries too.

Conclusions:
Confidential enquiries of rare disorders in pregnancy are valuable to get valid information about reducing risks and best treatment of complications and for deliveries in general. All professionals being involved in caring pregnant women could improve obstetric management, if suitable knowledge will be spread widely (guidelines). Therefore a surveillance-system including an internet-based information- and communication-platform will be established in Germany.

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Effects of gestational weight gain and body mass index on the risk of caesarean section in Portuguese women

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Objective: To estimate the association between gestational weight gain, in different maternal body mass index (BMI) classes, and caesarean section (elective and urgent).

Methods: The analyzes included 8300 women who delivered a term singleton live born between June 2004 and September 2007. Information on maternal characteristics was collected from medical database at hospital admission of women for delivery. Women were grouped in five categories of BMI and in five categories of gestational weight gain: ≤4kg, 5-8kg, 9-12kg, 13-16kg and ≥17kg. Associations between BMI categories, gestational weight gain and caesarian section (CS) were adjusted through logistic regression analysis for maternal age, number of pregnancies, previous caesarean, gestational age and birth weight for gestational age. The urgency and indication for CS was registered in the database by the performing obstetrician.

Results: The risk of CS increased with the increase of BMI pre-pregnancy. Gestational weight gain less than 5kg or higher than 16kg were associated with significantly higher risk of CS. This relationship was more evident for urgent CS. Obese women with low gestational weight gain had an increased risk for CS. The increased risk of CS among women with less gestational weight gain is due to the obese women who gain very low weight during pregnancy.

Conclusions: The influence of gestational weight gain on the risk of CS is largely dependent on maternal BMI. Since anthropometrics differ among pregnant populations, International guidelines recommending weight gain should be carefully evaluated before clinical use.

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Second trimester inflammatory markers in pregnant women with and without gestational diabetes

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Background and Aims: Recent evidence suggests a possible relationship between inflammation and gestational diabetes mellitus (GDM). We aimed to investigate C reactive protein (CRP), White blood cell count (WBC), and sedimentation levels as markers of subclinical inflammation in pregnant women with and without GDM in the second trimester.

Methods: 55 women with GDM and 55 women with normal glucose tolerance (NGT) with a mean gestational week 26.3 and 25.8 respectively were included in the study. Clinical and anthropometric characteristics were recorded. Serum high sensitive CRP, WBC, sedimentation, fasting glucose and insulin were measured.

Results: Fasting glucose levels were high in the GDM group (p<0.001) None of the serum levels of hsCRP, WBC and sedimentation did not differ between the groups of GDM and NGT. The mean hs CRP was 5.46 in the GDM group and 6.6 in the NGT group (p=0.30) WBC levels were 10.464 and 12.421 between GDM and NGT respectively (p=0.34) Sedimentation rate 34.9 and 37.5 between GDM and NGT respectively (p=0.44) Insulin levels were not also different between the groups (p=0.905)

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Introduction: The findings showed that obese women had the highest risk of suffering of pre-eclampsia and there is no positive correlation with the newborn birth-weight. The aim of the study is to show complications during the pregnancy and their deliveries in patients with more than 15kg gaining during pregnancy.

Materials and methods: The study looked at 2369 history of illness/delivery in patients who gave birth in General Hospital in Kumanovo in period 2006/07/08. They gaining more than 15kg during the pregnancy.

Results: Pregnant women from areas of lower socioeconomic status had higher prevalence of overweight than women from areas of higher status. Anyway relationships were found between overweight women and increased risk of pregnancy complications: 52 patients with preeclampsia, 389 with hypoproteinemia, 112 acute Caesarean Section, low birth weight newborns 31.

Conclusions: Overweight during the pregnancy was predictor of pregnancy/delivery complications.

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Neonatal and maternal outcomes in pregnancy complicated by GDM and pathological obesity: Efficacy of the intensive treatment

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Abstract: We evaluated the effects of an intensive multidisciplinary treatment of gestational diabetes mellitus (GDM) on the incidence of perinatal complications. Methods: The study included a cohort of 107 infants born between Jan. 2007 and March 2009 in our hospital. The mothers had been diagnosed and intensively treated GDM before than 30 weeks’ gestation. They received dietary advice, were instructed on self blood glucose monitoring and insulin therapy was initiated for fasting and/or 1 h post-meal glucose higher than 100mg/dl, and 125mg/dl respectively. Visits were planned every 2 to 3 weeks (more frequently if needed); the diabetes team was available daily for phone consultation. Maternal data and neonatal outcomes are shown in the Table.

<table>
<thead>
<tr>
<th></th>
<th>Overall (104)</th>
<th>Obese (34)</th>
<th>Non Obese (70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregestational BMI</td>
<td>26.9±5.9</td>
<td>34.1±3.7</td>
<td>23.6±2.9</td>
</tr>
<tr>
<td>Ponderal increments at delivery</td>
<td>10.7±4.8</td>
<td>7.6±4.8</td>
<td>12.1±4.1</td>
</tr>
<tr>
<td>GA at diagnosis/ GA at delivery</td>
<td>25.6±6.6/37.9±1.9</td>
<td>22.9±7.5/37.5±2.2</td>
<td>26.9±5.7/38.3±1.7</td>
</tr>
<tr>
<td>Insulin therapy N (%)</td>
<td>82 (79)</td>
<td>30 (88)</td>
<td>52 (74)</td>
</tr>
<tr>
<td>Gest.Hypert.(/)/Pregest.Hypert.(/)</td>
<td>9 (8)/ 3 (2.9)</td>
<td>5 (15)/ 2 (6)</td>
<td>4 (6)/ 1 (1.4)</td>
</tr>
<tr>
<td>Caesarean Section (%)</td>
<td>51 (49)</td>
<td>18 (53)</td>
<td>33 (47)</td>
</tr>
<tr>
<td>Newborns Total (couples of twins)</td>
<td>107 (3)</td>
<td>35 (1)</td>
<td>72 (2)</td>
</tr>
<tr>
<td>Neonatal Transitory Tachipnea TTN 6</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>NICU admission (RDS)</td>
<td>1</td>
<td>1#</td>
<td>0</td>
</tr>
<tr>
<td>Hypoglycemia (&lt;30mg%) (1°h)</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Ponderal Index</td>
<td>2.6±0.3</td>
<td>2.57±0.2</td>
<td>2.65±0.3</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>4.7±3.4</td>
<td>5.8±4.9</td>
<td>4.1±2.7</td>
</tr>
</tbody>
</table>

Conclusions. The intensive multidisciplinary treatment of GDM improves neonatal outcomes and reduce maternal and fetal complications with Results similar to physiological pregnancy also in pregnancies complicated by pathological obesity.

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Maternal obesity and pregnancy outcome

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Objective:
The obesity is a chronic disease with a marked increase in the last decade. Several studies have reported that maternal obesity is associated with increased risk of adverse pregnancy outcomes. We want to describe the pregnancy outcome in our obese pregnant.

Methods:
It is a retrospective study of 63,119 pregnant women with a labor in our hospital from the year 2000 to the 2008. 9,635 women were obese. We define obesity as body mass index equal or greater than 30. We considered the first prenatal visit maternal weight. The women with labor before 24 weeks of pregnancy or without weight or height data were discarded.

Results:
Outcome: Obese group (n=9,040) vs. Control group (n=54,079)
Macrosomia: 925 vs. 2,690 (RR: 2.06 CI 95%: 1.92-2.21)
Stillbirth: 63 vs. 277 (RR: 1.36 CI 95%: 1.04-1.79)
Low Apgar score (<7): 76 vs. 275 (RR: 1.65 CI 95%: 1.28-2.13)
Admission to neonatal intensive care unit (NICU): 133 vs. 626 (RR: 1.27 CI 95%: 1.06-1.53)
Caesarian section: 1,834 vs. 6,650 (RR: 1.65 CI 95%: 1.57-1.73)

Conclusion:
The risk for macrosomia, stillbirth, low Apgar score, admission to NICU and caesarian section was more common in the obese group.

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Effects of Betamethasone in gestational diabetes screening

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Introduction: Antepartum betamethasone administration between 24 and 34 weeks is known to reduce neonatal morbidity and mortality, but is believed to induce a maternal diabetogenic state, which can lead to falsely positive Results in gestational diabetes screening.

Objective: To determine if betamethasone significantly alters 50g-glucose challenge test Results in pregnant women.

Material/Methods: A prospective study was conducted between July 2008 and March 2009. All women admitted between 24–34 gestational weeks, to which betamethasone had been prescribed and gave informed consent, were included. Women in active labor, with infectious, hepatic or pancreatic disease, or under prolonged corticosteroid or β-mimetic therapy were excluded. 50g-glucose challenge test was performed immediately before betamethasone administration and 24h and 72h after. Women with positive 50g-glucose test (≥140mg/dL) before betamethasone were excluded. Those with positive 50g-glucose test at 72h underwent 3 hour oral 100g-glucose tolerance test. For statistical analysis Student t-test was used (α=5%).

Results: A total of 27 women were enrolled, and 15 women completed the study. Mean value of blood glucose after 50g-glucose challenge test was higher at 24h (p<0.001) and 72h (p=0.031) after betamethasone administration. Four 50g-glucose challenge test Results were positive at 72h; nonetheless, the 3 hour 100g-glucose tolerance test was negative in all of them.

Conclusion: Previous studies suggested a potential role of betamethasone in raising blood glucose. Our study confirms a raise in mean blood glucose values after betamethasone administration, but no diagnosis of gestational diabetes was made.

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Echocardiographic findings of congenital cardiopathies among fetuses whose mothers had diabetes and their relationship with frutosamine plasma levels

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Objectives: To study the occurrence of congenital cardiopathies at echocardiography (CCE) in fetuses whose mothers had preexisting or gestational diabetes mellitus (DM) and to associate plasma levels of frutosamine during pregnancy with CCE. Methods: A register study covering 126 pregnant women (30.9±6.7 years old), from 2000 to 2007, that were submitted to routine fetal echocardiography by the same physician, indicated because of DM during pregnancy. We analyzed the first dosage of plasma frutosamine during prenatal care (22.6±8.3 weeks of gestation) that was found in 79 medical records. The presence or absence of structural or functional CCE was associated with frutosamine plasma levels by logistic regression. We assessed odds effect modification by maternal age. Results: Sixty eight fetuses (64% of the 126 fetus) presented CCE. Forty nine (72%) had structural CCE, 8 (11.8%) had functional CCE and 11 (16.2%) presented both. Among structural CCE, cardiomegaly of any cardiac chamber was the most frequent (70%), followed by interventricular communication (35%). Among functional ones, the most frequent was pericardial effusion (58%), followed by bradycardia (37%). The mean maternal frutosamine plasma level was higher among pregnant women whose fetuses presented CCE than in those whose fetuses did not (2.72±0.81mmol/L, 2.17±0.57mmol/L, respectively, p<0.0001). Crude OR for CCE and abnormal plasma frutosamine (>2.68mmol/L) was 5.48 (1.6-18.0, 95% CI, p=0.0008). Adjusted OR by maternal age was 5.7 (1.8–17.9, 95% CI p=0.003).

Conclusions: DM was associated with CCE. An abnormal frutosamine plasma level increases the chances of having CCE. Supported by FAPEMIG

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Obstetric history and obstetric complications of women delivering extremely low birth weight infants

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Objectives To describe the obstetric history and obstetric complications of women delivering infants with a birth weight ≤750 gram (g). To compare these variables between two consecutive five year periods and between small for gestational age (SGA, ≤p2.3) and appropriate for gestational age (AGA, >p2.3) infants. The question was raised whether being born with a birth weight ≤750g can be prevented.

Methods A retrospective cohort study of 272 infants with a birth weight ≤750g and gestation of ≥24 weeks, born between January 1996 and January 2006, assessing maternal characteristics and neonatal outcome.

Results In 84.4% of the multigravids a complicated obstetric history was found; 44.5% had spontaneous abortion (s) and 24.2% a preterm delivery. In the index pregnancy the most prevalent obstetric complications were hypertensive disorders (52.1%), intrauterine growth retardation (IUGR) (80.8%) and fetal distress (40.2%).

Conclusions Only 15.6% of our maternal population delivering infants with a birth weight ≤750g had an uncomplicated obstetric history. The most prevalent obstetric complications in the index pregnancy were pregnancy related hypertensive disorders and concomitant placental insufficiency and intrauterine growth retardation, whereas the prevalence of a spontaneous preterm birth occurred in a minority. We conclude that birth of infants with a birth weight ≤750g can rarely be prevented.

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Impact of body mass index on gestational diabetes melitus

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Objective: To assess the impact of BMI in the treatment and perinatal outcome of patients with GDM.

Methods: A retrospective cohort study was carried out. Participants of this study were 258 pregnant women suffering from GDM and their newborn infants. The women were divided into 4 groups: low (BMI<18.5kg/m2), normal weight (BMI between 18.5 and 24.9kg/m2), overweight (BMI 25-29, 9kg/m2) and obesity (BMI> or =30kg/m2). The study was carried out from January 2003 to March 2008. Data related to diabetes and the newborn was evaluated.

Results: Patients were found to be 10.1% low weight, 63.9% normal weight, 12.4% overweight and 13.6% obese. According to the variables related to DMG, an increase in fasting blood glucose with OGTT and in fasting home glycemic control corresponded to an increase in BMI (p<0.05), but this has not occurred after 2hs OGTT or postprandial home glycemic control (p>0.05). The need of using insulin as therapy occurred regardless of the patient's BMI (p=0692), however, insulin doses increased with BMI (p=0053). Regarding characteristics of birth and the newborn, no differences between the 4 groups were found.

Conclusion: As BMI increased, a rise in fasting blood glucose with OGTT, in fasting glycemia collected during treatment, and in the final dose of insulin was found. However, no effect in newborns was found in relation to this index.

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Antiphospholipid syndrome during pregnancy

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Patient 29 years old, in her first pregnancy, at 30 weeks of pregnancy, is admitted to our Hospital with a neurological disorder (disorientation, amnesia and agitation). The ultrasound explorations shows a pathological, umbilical Doppler study and fetal growth restriction. The blood analysis shows a low platelet count and prolonged PT Ta.

A brain CAT scan and MRI is carried out which shows an image of ischaemic infarction alteration in the subcortical level in the right frontal lobe.

The study for thrombofillia is positive for antiphospholipid syndrome and negative for lupus.

At 31 weeks of gestation a caesarean section is carried out because of the fetal growth restriction and the pathological Doppler study. Antenatal steroid therapy for fetal lung maturation was complete.

Newborn female, 1,070g, Apgar's score 8/9.

Anatomopathologic study of placenta show two ischaemic areas and haemorrhage.

The evolution of the patient after delivery is satisfactory with an improvement in the neurological symptoms and analytic disorders with anticoagulant treatment and steroid therapy.

The evolution of the newborn is satisfactory as well, without evidence of neurological disorders or lung pathology for prematurity and low fetal weight.

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Severe thrombocytopenia during pregnancy

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Introduction: Maternal thrombocytopenia is a frequent finding in pregnancy. Severe thrombocytopenia with a platelet count of lower than 50 x 10(9)/L is rare, occurring in less than 0.1% of pregnancies. The clinically important causes of maternal thrombocytopenia in pregnancy are gestational thrombocytopenia and autoimmune thrombocytopenia. Although it affects only 1 to 3 per 1,000 pregnancies, idiopathic thrombocytopenic purpura has received attention in the obstetrics literature because of the potential for profound neonatal thrombocytopenia in infants born to mothers with this condition.

Case report: We report a case of a 33-year old primigravida referred to our department at 37 weeks of gestation because she presented a platelet count of 6 x 10(9)/L, epistaxis and petechiae. She had a history of idiopathic thrombocytopenic purpura and was medicated with deflazacort. She was successfully treated with high dose corticosteroids and immune globulins. She had a vaginal delivery without complications at 38th week of pregnancy and a normal puerperium. The male infant of 2,940g, with an Apgar score 10/10, had no signs of neonatal thrombocytopenia.

Conclusion: The challenge to the clinician is to weigh the potential adverse effects of the treatment for the woman and/or the fetus against the requirement for a good hemostasis at delivery and the risk of neonatal hemorrhage.

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Trombophilia screening during pregnancy: performance of a brief clinical history

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Objective: To analyze the performance of a short clinical history focused on the detection of acquired and inherited trombophilia risk factors.

Material and Methods: A systematically question “Have you or any of your first-grade relatives, ever had an episode of thrombosis, stroke or heart attack under the fifties?” were asked to all pregnant patients in the first gestational control. Personal precedent of early onset IUGR or preeclampsia, intrauterine death or abruption placenta, was also considered a risk factor.

Results: A total cohort of 342 consecutive women was polled. The answer was affirmative in 33 (9.6%), so screening blood test for acquired and inherited thrombophilia was performed. Risk group ethnic origin was Caucasian in 26 (78.8%), and mean age was 29.4 years. Risk factors were: 1) first-grade relative thrombotic event in 61% (stroke 23%; heart attack 27%; deep vein thrombosis 11%); 2) gestational precedents in 36% patients (early-onset IUGR-Preeclampsia 18%, intrauterine death 14%, abruptio placenta 4%); and 3) personal previous thrombotic event in 3%. Screening test was positive for at least one type of thrombophilia in 25 (75.7%) patients, and 9 (27%) presented both acquired and inherited thrombotic disorders. Acquired thrombophilia was found in 15 (45.4%) women (S Protein deficiency 36%, Increased Factor VIII 16%, Lupic anticoagulant 8%). Inherited thrombotic disorders were detected in 22 patients (Heterocigous MTHFR C677T (25), Homocigous MTHFR C677T (10), Homocigous MTHFR A11298C (6)).

Comment: A brief focused clinical history is an easy and effective screening tool for thrombophilia during pregnancy.

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Prevalence and risk factors for anemia in pregnant women of south-east Iran

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Objectives: To study prevalence and risk factors of women with anemia during pregnancy in south-east Iran.

Methods: A retrospective cohort study was performed based on 2223 pregnancies delivered during the years 2005-2007 in Kerman, Iran. Women with hemoglobinopathies such as thalassemia were excluded from analysis. Anemia was defined as hemoglobin (Hg) lower than 11g/dl during pregnancy. Categorical variable were compared using the chi-square or Fisher's exact test.

Results: Overall, 104 (4.7%) of the study population were anemic (Hg<11g/dl), 4.8% had severe anemia (Hg<7g/dl), 15.4% had moderate anemia (Hg=7-8.9g/dl) and 79.8% had mild anemia (Hg=9-10.9g/dl). The frequency of anemia at different trimesters were 5%, 3.4% and 5.7% in the first, second and third trimester, respectively. Multiparty, smoking, opium use and preterm delivery was associated with anemia.

Conclusion: Our study showed that prevalence of anemia was not high in this study. Factors associated with anemia during pregnancy were parity, smoking, opium use and non-iron use.

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Clinical experience in treatment of severe postpartum anemia with ferric carboxymaltose

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Introduction: Postpartum anemia is a common obstetric problem - up to 30% of pregnant women suffer from iron deficiency anemia. This situation is worsened by considerable blood loss during childbirth. Blood loss stimulates erythropoiesis, which, to be successful, requires the presence of mobilizable iron reserves. Anemia due to iron deficiency contributes to several postpartum morbidities such as lethargy, lactation failure, cognitive impairment, and postpartum depression (1). Although most women are treated with oral iron supplements to replenish the depleted iron stores, the utility of oral iron is limited by gastrointestinal complaints and patient nonadherence (2). Intravenous iron also has limitations due to irritation at the injection site and limited absorption rate.

Methods: To meet this clinical challenge we established a protocol at the department of Obstetrics and Gynecology at the Ludwig-Maximilians-University for the treatment of severe postpartum anemia with intravenous ferric carboxymaltose. All patients with a blood loss of greater 1000cc or a postpartum hemoglobin level below 7g/dl were treated with ferric carboxymaltose according to the manufacturer`s guidelines.

Results: Since June 2008 we have treated ten patients with severe postpartum anemia. Median predelivery Hb was 9.5g/dl, median blood loss 1950 cc. Median hemoglobin levels before treatment were 5.8g/dl; two to three weeks after treatment they rose to 10.6g/dl. Patients reported significantly improved quality of life with no side effects.

Conclusion: Ferric carboxymaltose is a new, very effective and safe drug for treating severe postpartum anemia.

Anti-thrombotic treatment in recurrent pregnancy losses

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Recurrent pregnancy loss is a common problem in women (1-5%). One of the leading causes is inherited thrombophilia. We enrolled 361 women (25-38 years-old) with history of at least two abortions due to unknown causes. We study the efficacy of three different antithrombotic treatments, comparing the Results in negative and positive thrombophilic patients.

For congenital thrombophilia we studied inhibitors of coagulation (antithrombin, protein C, protein S), Factor V and Factor II (G20210A) mutations. Lupus Anticoagulant (KCT, DRRVVT), Anticardiolipin antibodies and homocysteinemia were considered for acquired thrombophilia. The screening identified 246 negative (68%) and 115 positive (32%).

167 women became pregnant, 80 (48%) negative and 87 (52%) positive. From eight weeks’ gestation they were submitted by three different therapy groups: Acetyl salicylic acid (ASA) 100mg/die until 3rd month of pregnancy; low molecular-weight heparin (LMWH) 40mg/die until 3rd month of pregnancy; ASA100mg plus LMWH 40mg/die until 3rd month of pregnancy.

In the 80 negative patients, all three anti-thrombotic regimens were statistically significant effective respect previous untreated pregnancies: 69 live births (86%) versus 11 abortions (14%) (p<0.0001)

In the 87 patients positive, the treatment with and LMWH combined ASA was statistically significant effective respect to previous untreated pregnancies: 58 (67%) live birth versus 29 abortions (33%) (p<0.001). Regimen with ASA alone did not shows any efficacy regarding pregnancy outcome.

We suggest that thromboprophylaxis is indicated in women with previous pregnancy loss independently from alterations of thrombophilic factors.

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Effect of substitution therapy on the birth weight of newborns, postpartum adaptation, trophism and course of the neonatal abstinence syndrome

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Included in the study were heroin-addicted pregnant women and pregnant women undergoing methadone and buprenorphine substitution therapy. During the 3 years we concentrated 47 heroin-addicted women and 60 women under substitution therapy for prenatal screening. 36 pregnant women were methadone-substituted and 24 buprenorphine-substituted. We monitored the effect of substitution therapy using two different preparations on duration of pregnancy, birth weight, the newborn’s early postpartum adaptation, development of IUGR and placental changes, NAS development, its severity and duration of its necessary therapy. The two groups (methadone and buprenorphine) were compared with the heroin-addicted pregnant women and with each other. Birth weight of newborns was statistically significantly lowest in the group of heroin-addicted women as compared to the group receiving substitution with buprenorphine p<0.01 and as compared to the group of methadone-substituted patients p<0.05. Physiological weight loss by 3rd day after the birth was higher in methadone- (p<0.01) and buprenorphine- (p<0.05) substituted women as compared with heroin users.

The statistically highest number of changes in the placenta was exhibited by heroin users, both when compared to methadone users (p<0.01) and buprenorphine users (p<0.001). Comparison of the two groups receiving substitution therapy showed statistically significantly more changes in the placenta of methadone-substituted women (p<0.001). The highest statistically significant number of newborns with IUGR symptoms were born to heroin-addicted women, namely when compared to the group of methadone users p<0.001 and to buprenorphine users p<0.05. No statistically significant difference between the groups under substitution therapy was found in the incidence of hypotrophic newborns.

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Pregnancy and addiction to recreational drugs -6 years Retrospective study

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(3) Hospital Of Faro, Paediatric, Faro, Portugal

Introduction:
Drug abuse during pregnancy is a major Public Health problem due to serious adverse consequences, both to mother and child.
Helping the pregnant women organize her life, if possible without drug abuse and minimize the fetal damages is the main goal of the clinical practice in the "Women Appointment of CAT Sotavento/Olhão".

Methods:
Retrospective analysis of clinical files from all drug addicted pregnant from 2003 to 2008 that gave birth at the Hospital of Faro – Gynecology/Obstetric Department.

Results:
There were 99 deliveries and 31 abortions, 20 of which voluntary.
The mother’s average age was 28.88 years.
58% did not do any contraception previously and those who did it, only 9% used condom.
The 1st doctor’s attendance was in average at 16 week; there were 10 women without pregnancy surveillance.
It was taken in count the abuse of cannabis, cocaine and heroin, being the average age of beginning of abuse: 16, 20 and 19 years old, respectively.
Despite 77% were going through a detoxification programme with methadone, 59% maintained drug abuse.
48% had HCV and 9% HIV.
The delivery was mainly vaginal at 38 weeks and most of the children stood 2 to 5 weeks at the Neonatology Unit.

Conclusions:
Despite poor maternal health, malnutrition, infectious diseases and polydrug abuse, our new born outcome was surprisingly good.
In the world of drug abuse, living several difficulties, the drug addicted pregnant is capable of managing her own risks and live/feel a responsible motherhood.

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Induction of Buprenorphine in pregnant opiate addicts

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In our institution approximately 50 pregnant opiate addicts are counseled every year. Following the work of Fischer et al. who described a reduction of neonatal opiate withdrawal following bupernorphine (BUP) maintenance therapy we have started to induce some our patients to a BUP maintenance therapy during pregnancy. In our presentation we report on more than 70 BUP inductions during pregnancy. We conclude that BUP-induction and maintenance during pregnancy is feasible and as safe as methadone maintenance therapy.

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Illicit substance abuse during pregnancy: Obstetric and perinatal outcomes

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Objective: To assess obstetric and perinatal outcomes of pregnancies burdened with maternal addiction at a tertiary care center.

Patients & Methods: A retrospective analysis of 47 pregnancies in women using illicit drugs between July 2001 and September 2008 was performed. Maternal, obstetric and perinatal outcomes were analyzed. Data on 100 non-dependence pregnancies managed during the study period were used as a control group.

Results: Polidrug use of heroin, cocaine and/or marijuana was found in 40 women (85.1%), 55.3% maintained drug abuse during pregnancy. Thirty-seven women (78.7%) were submitted to methadone therapy. Nineteen pregnant addicts (40.4%) were carriers of hepatitis C virus, 3 (6.4%) of hepatitis B virus and 5 (10.6%) were infected with HIV; 10 (21.3%) had sifilis. There was a significant higher preterm delivery rate in the drug abuser group (29.8% vs. 8.0%, P=0.002). The incidence of placental abruption and intrauterine growth restriction were also significantly higher among pregnant addicts. When compared to the control group, their infants were more significantly likely to be small for gestational age. Congenital malformations were detected in 6.4%(3) of cases, 2 of which resulted in termination of pregnancy. Twenty-eight of 45 neonates (62.2%) developed neonatal abstinence syndrome and in 5 (11.1%) congenital sifilis was suspected.

Conclusion: Illicit substance abuse during pregnancy is associated with adverse obstetric and perinatal outcomes. Appropriate strategies of pregnancy management and neonatal care should be defined in this high-risk group, in order to reduce obstetric complication rates and improve perinatal outcomes.

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Objective: Our purpose was to determine maternal and fetal outcome in patients undergoing surgery for a pelvic mass in pregnancy. Maternal and fetal records (outcomes) of 31 cases of adnexal masses associated with intrauterine pregnancy from 1994 to 2008 that required laparotomy or aspiration or that was diagnosed incidentally at the time of caesarean section were reviewed. We included patients with simple or complex masses \( \geq 6 \text{cm} \) that were persistent on ultrasonographic evaluation and patients with adnexal masses with complications (torsion, haemorrhage, incarceration). Patients with cysts that spontaneously resolved by 16 weeks' gestation we excluded.

Results: 31 patients of 33 147 deliveries were identified with adnexal masses that satisfied the above criteria. In seven patients out of ten with acute symptoms laparotomy was done. Remaining three patients underwent transvaginal aspiration of simplex cyst due to subtorsion two in the first and one in the second trimester of gestation (negative Results on cytological study). Twenty out of 21 patients without acute symptoms underwent laparotomy and in one transvaginal aspiration was done. One epithelial borderline malignant mass and 28 benign ovarian tumors were found. Out of all 31 patients 28 patients had deliveries (26 terms and 2 preterm's) and one patient had abortion. Two patients were lost from follow up. Conclusion: There were no differences in pregnancy outcome between emergency and planned surgery. We emphasize that transvaginal aspiration and drainage of symptomatic simplex cysts in the first trimester and percutaneous cysts in the second trimester can avert laparotomy.

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Ovarian vein thrombosis (OVT) is an uncommon but potentially serious complication in the early postpartum.  

Case 1: A 24-year-old woman was transferred to our hospital with the chief complaint of abdominal pain radiated to the right thigh, vomit, diarrhea and a slightly pyrexia (37.6°C rectal). Five days before, she had a spontaneous vaginal delivery after labor induction. The woman appeared slightly distressed because of pain, vital signs were normal, CRP elevated (129.9mg/L). Abdominal examination was remarkable for tenderness by palpation in the right lower quadrant with no rebound tenderness or guarding. Pelvic examination was remarkable for mild right adnexal tenderness. Abdomino-pelvic CT with contrast medium revealed a 2.5cm OVT extended into the inferior vena cava for 14cm with a slightly peripheral edema. The patient was treated with nadroparin 0.6cc (5700IU) bid and Warfarin 5mg since achievement of the therapeutic INR range.

Case 2: A 31-year-old twin-pregnant woman had an emergency caesarean section at 35 gestational weeks because of hypertension complicated by increased liver enzymes, diuresis contraction and continuous low back pain bilaterally radiating to the groins. One day after delivery, because of onward anemia, CT scan was performed, which showed a pelvic, perihepatic and perisplenic blood effusion, and a 1cm right OVT extended to the inferior vena cava below renal veins for 28mm. She underwent exploratory laparotomy and emotransfusion, and transferred because of respiratory insufficiency to a second level center with ICU facility, were it was placed a suprarenal inferior vena cava filter and AngioJet Rheolytic Thrombectomy for acute pulmonary embolism was performed.

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Phaeochromocytoma during Pregnancy

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Introduction: Phaeochromocytomas are tumors of the adrenal medulla, found in 0.1% of non-pregnant patients with hypertension, but are rarely encountered (<200 reports) in pregnancy. When undiagnosed, maternal and fetal mortality are high. Phaeochromocytomas are in 10% bilateral, in 10% extra-adrenal and in 10% malignant.

Case: We report on a 31 year-old Gravida 3, Para-0 who was transferred at 17 weeks with severe hypertension of 185/100 and symptoms of headache and maternal tachycardia. Before pregnancy, she was treated by ACE-inhibiting drugs and diuretics. As soon as pregnancy was diagnosed methyldopamine was administered instead. At admission, sonograms of the adrenals were normal and there were no signs of stenosis of the renal arteries. Laboratory values were all within the normal range. Urine controls found a 1.5 fold increase of noradrenalin, a 3-fold increase of dopamine and a 6-fold increase of adrenalin suggesting a phaeochromocytoma. MRI demonstrated a knot of 10mm in the right ganglion stellatum confirming the diagnosis of a phaeochromocytoma. After administration of a selective alpha1-blocker her blood pressure stayed within the normal range.

Uterine and fetal blood flow as well as fetal growth were normal. The mother decided to continue pregnancy after informed consent. The team was instructed of all emergency actions including treatment of a hypertensive crisis.

Conclusion: Women with hypertension associated with unusual features of palpitations, anxiety, sweating, headache or glucose intolerance should be investigated for signs of phaeochromocytoma. Alpha blockade for at least 3 days prior to surgery is recommended.

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Breast cancer during pregnancy. A case report

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Introduction: Pregnancy associated breast cancer (PABC) is the second most common malignancy diagnosed during pregnancy with an incidence of 1:3,000. We present a case in the third trimester to evaluate optimal treatment.

Case report: A 41-year-old patient, gravida 4, para 4, normal pregnancy, was presented at 29 weeks with a palpable tumor in the left breast. A fine-needle biopsy showed invasive ductal carcinoma. No metastases. She initially had a mastectomy with axillary lymph node dissection in the 30th week (histology stage: pT2, pN1a (3/26), M0, G3, ER negative/PR 30%, HER-2neu 1+) Normal postoperative course and fetal well-being. After induction of labor in 35 weeks a male baby with Apgar scores of 9 at both 1 and 5 minutes was born by vacuum extraction. Beginning one week postpartum the patient was given 3 cycles of adjuvant chemotherapy using 5-flurouracil, epirubicin, and cyclophosphamide (FEC), followed by 3 cycles of docetaxel, sequential application of tamoxifen/goserelin, and radiotherapy. To date the patient has been cancer-free for two years. Her baby is doing well.

Conclusions: PABC poses unique management challenges to an interdisciplinary care team, specifically maximizing the survival of the mother balanced with the health of the fetus. Although data are limited, pregnant patients can be treated with systemic chemotherapy with minimal risks to the fetus during the second and third trimester. According to the patient’s preference the chemotherapy was planned after delivery. Therefore an induction of labor calculating the risk of prematurity was performed. The management requires a careful consideration of the preferences of the patient and her family.

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Optimizing perinatal care for patients obtaining immunosuppressive therapy

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Exposure to immunosuppressant agents (IS) and their metabolites during gestation has been associated with increased risk of complications for both the mother and the child. Gestational complications include elevated occurrence of preeclampsia and gestational diabetes mellitus, aggravation of hypertension, preterm delivery, intrauterine growth retardation and prematurity, increased incidence of spontaneous abortion, and malformations, since IS can cross the placental barrier and thus interfere with fetal development. Immune function as well as neuronal development of those infants may be detected in the later childhood-period as well. On the other hand graft loss or aggravation of autoimmune disease of the mother may occur during pregnancy.

We created treatment-guide lines for women who receive immunosuppressant agents including optimal pre-conceptional preparation (changing of IS, vaccination, genetic evaluations, stabilization of organ function), peripartal care including (regularly ultrasound investigations, early and late organ screenings and fetal MRI scans with special focus to those malformations that are known to be associated with the administered IS, measurement of IS-levels and graft function, early detection of opportunistic infections, stabilization of blood-pressure, mode of delivery). Our guide lines for postpartum care include management of breast feeding, adjustment of IS and other medication, and special investigations of the newborn.

In conclusion, pre-, perinatal as well as postpartal care of women who underwent solid organ transplantation or who suffer from autoimmune disease and therefore administer IS needs intensive interdisciplinary perinatal care for mother and child following special guide lines in the setting of a specialized department for feto-maternal medicine.

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First trimester incidental abdominopelvic mass – case report of Ganglioneuroma in pregnancy

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Retroperitoneal Ganglioneuromas are benign lesions from the sympathetic autonomomic nervous system, thought to be the fully differentiated counterpart of neuroblastomas. Retroperitoneal ganglioneuromas are rare and usually asymptomatic, often casually diagnosed.

An asymptomatic 26 years old pregnant female presented with an incidentally discovered pelvic mass on her first trimester routine ultrasound. A large palpable mass occupied most of pelvis and left flank, with no other relevant findings. Echography showed an hypoechoic mass, with no significant vascularization and punctuate calcifications throughout, with over 20cm of larger diameter, apparently unrelated with the uterus and no visible left ovary. Further blood work, including oncogenic markers and image workup was unremarkable: MRI confirmed a large, possibly multiple or lobulated mass, was equally unable to observe the left ovary, and did not discard a retroperitoneal origin.

Given the extensive mass limited adequate fetal growth and development, the patient underwent laparotomy at 18 weeks pregnancy. Retroperitoneal masses were observed and six apparently capsulated lesions were excised, the largest of which had 20cm larger diameter. The deepest mass couldn’t be completely excised, by concerns of further blood loss, given close proximity with the pelvic vessels. Extemporaneous anatomopathological report by frozen section suggested ganglioneuroma, diagnosis which was later confirmed.

The patient recovered well and is currently on her 21st week of pregnancy; the fetus appears to be adequately growing and developing.

Further news on the pregnancy outcome are to be expected by the time of the congress.

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Melanoma during pregnancy: a diagnostic and therapeutic challenge

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A 30-years-old pregnant woman, tertigravida secondipara, overweight, with a familiar history of breast cancer, at 34 gestational weeks underwent surgical excision of a suspicious dysplastic nevo in the left latero-cervical region, after dermatologic consult.

Histologic examination made diagnosis of epithelioid hyperpigmented melanoma, “animal type” variant, pT3a, II stage by Clark, Breslow index (correspondent to papillar derma invasion) 2.1mm, mitotic index 5mitosis/10HPF (0.192qm), peri-tumoral but not intra-tumoral inflammatory reaction, and no margin involvement.

At 37 gestational weeks the women underwent labor induction in order to allow a prompt onchologic management, and spontaneously delivered a female newborn of 2,880gr. Although discouraged, the women successfully breastfed.

Neck ultrasonography revealed no reactive lymphnode. The sentinel lymph node biopsy after SPECT/TC detection resulted negative for metastasis, as also the toraco-abdominal CT. At the 6 months follow up, surgical scar was improving and there was no evidence of recurrence.

Pregnancy may accelerate melanoma development in predisposed women, apparently not affecting the prognosis.

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Case report of a successful pregnancy after radiotherapy for thyroid malignancy with 5 year follow up

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Introduction: Radioactive iodine has been used effectively in diagnosis and treatment of thyroid diseases. Since radiation is delivered to the whole body, including ovaries, it's a reasonable concern whether there is a possibility of mutagenic effect on germ cells.

Case report: We report a 33 year old woman admitted in the surgical department of our institution with a differentiated papillar carcinoma. According to preoperative examinations it was a T2N0M0 tumor. The woman underwent the radiotherapy 3 weeks after the surgery and one year after finishing her therapy she became pregnant. She had a normal and uncomplicated pregnancy and at the 38th week of gestation she delivered vaginally a healthy female neonate weighing 3100gr. The neonate at the age of five years is healthy with no signs of malignancy or other disease associated with radioactive therapy.

Discussion: Washout of 131I of the whole body takes place in a few days. Nevertheless, most guidelines recommend avoiding pregnancy for 4 to 6 or 12 months after RAI treatment or scanning. As reported in our case a normal uncomplicated pregnancy can follow an operative and complementary treatment of thyroid cancer.

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Treatment of ovarian border-line (BL) tumor in pregnant women

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Introduction: Borderline tumors of the ovary are epithelial proliferative non-invasive tumors with histopathology parameters between benign tumors and malignant neoplasms. Ovarian BL tumors represent 10-15% of all ovarian cancer with an yearly incidence of 0.004%-0.01%. The mean age at diagnosis is 40. Therefore their onset during pregnancy is not an exception. The overall 10 yrs survival is 83-91%.

Methods: From 1990 to 2006 we studied 169 cases with a diagnosis of serous or mucinous ovarian BL tumor. The patients’ age ranged from 17 to 83 years (median 43 years old). 75 patients (44%) were younger than 40 yrs, 5 of them (6.6%) were pregnant and had stage IA disease at the time of diagnosis. (3 serous, 2 mucinous histotype).
All five women underwent laparotomic or laparoscopic surgery: four of them underwent conservative surgery, one underwent bilateral salpingo-oophorectomy.
All the patients gave birth to healthy children, 2 delivered spontaneously, 3 underwent caesarean section. (1 placenta previa; 1 podalic presentation; 1 iterative CS)
3/4 patients who underwent conservative fertility-sparing surgical treatment conceived within the next 5 years.
All five patients, after a follow-up ranged from 97 to 193 months (median 146 m.), were alive with no evidence of disease. None of them developed recurrent tumour.

Conclusions: Conservative surgery should be considered for patients who wish to preserve fertility and offered to young patients (<40 years) with early stage (I-II) disease. This treatment could also be considered appropriate during pregnancy to preserve the health of mother and the pregnancy outcome

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Mechanical valve protheses and pregnancy: complication and outcome

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Introduction: Pregnancy in women with mechanical valve prostheses has high rates of adverse outcomes. Valve thrombosis (VT) is a serious complication and needs special management.

Casuistic: We report a case of a 30 year old pregnant woman GIV PI with a mechanical valve replacement in aortic position 1989 and a replacement in aortic and mitral position 2000. She had a vaginal delivery 1999 under treatment with low-molecular-weight heparin (LMWH) 15000 U/24h and 2 abortions. In 2007 Vitamin-K-antagonist (VKA) treatment was replaced in early pregnancy by 15000 U/24h LMWH. In the 9th week of gestation (WG) she developed acute heart failure with cardiogenic shock, echocardiography demonstrated VT in mitral position. She was anticoagulated with therapeutic unfractionated heparin (UFH) and received systemic thrombolysis with rt-PA 100mg twice in 24h with successful lysis of the thrombus. UFH was continued until the 12th WG. Treatment was then changed to VKA until two days before delivery. Due to cardiac decompensation caesarean section with good fetal outcome was performed in the 36th WG. Postpartum she received UFH and VKA and had to undergo operative revision of a subcutaneous hematoma.

Conclusion: VKA are relatively safe for the mother with a low incidence of VT but carry the risk of embryopathy. LMWH and UFH are safe for the embryo but need close dose-adjustment throughout pregnancy. Thorough evidence for the efficacy of LMWH is still lacking and this is an issue of debate, clearly stressing the need for a close interdisciplinary monitoring of these high risk pregnancies.

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Maternal and perinatal complications in women with congenital heart diseases

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Purpose: To Evaluate the occurrence of perinatal and maternal complications (clinical and obstetrical) in pregnancies of patients with congenital heart diseases (CoHD).

Methods- Retrospective analysis of clinical and obstetrical complications rates and data from 165 newborns of 162 pregnancies of women with CoHD between may-2001 and April-2005.

Results: 46.6% of patients had a previous cardiac surgery and 2.5% had complex cyanotic CoHD not submitted to previous surgery. We observed the following events: obstetrical complications in 28.3% and clinical morbidity in 20.37%; functional class III or IV (NYHA) of heart failure in 12.9%; use of cardiovascular drugs in 34.4%; caesarean section in 64.4% of pregnancies (obstetrical indication in 70% and general anesthesia in 40% of caesarean deliveries). The gestational age in the delivery was 37.9±2.2 weeks (17.8% <37 weeks). One woman (0.6%) with Eisenmenger syndrome died in the puerperium period. Data of newborns: mean weight 2,858±590grs (27.3% babies small for gestational age; and 23% under 2500grs). We did not observe early perinatal death. Apgar of 1st e 5th minutes <7 occurred in 12.2% and 1.8% respectively; 8.4% of newborns needed intensive care unity after delivery and 6.6% needed orotracheal intubation in the delivery room.

Conclusion: Pregnancy in patients with congenital heart disease, although safer than previously observed, had elevated rates of maternal and fetal complications.

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Pregnancy in a woman with congenitally corrected transposition of great arteries- case report

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Congenitally corrected transposition of the great arteries (CTGA) is an uncommon form of congenital heart disease characterized by atrioventricular (AV) and ventricular great arterial discordance, which accounts for <1% of all congenital cardiac defects. During pregnancy substantial hemodynamic changes happen and may adversely affect the hemodynamic status of a woman with CTGA.

The authors present a case of a 29 years old pregnant nulliparous woman with a congenitally corrected transposition of the great arteries (CTGA) previously submitted to corrective surgery at 11 years old by valvuloplasty of AV valve with Carpentier ring.

Prior to pregnancy she was followed by a cardiologist where an asymptomatic tricuspid insufficiency was diagnosed. During pregnancy serial echocardiograms were performed which revealed no deterioration of her previous condition. There was no need for medication during pregnancy.

Cesarean section was performed at 35 weeks gestational age due to uterine contractility, with endocarditis antibiotic prophylaxis given during the procedure. No hemodynamic alterations occurred during the labor in the mother. A 2,280g normal female newborn was delivered. The child initiated a respiratory distress syndrome and as so, was admitted in the intensive care unit for ten days. No cardiovascular anomaly was found in the child.

Five months after birth, maternal cardiac function remains the same as before pregnancy.

Women with CTGA often reach child bearing age and have a propensity for congestive heart failure and cardiac dysrhythmia during pregnancy, labor and delivery. Few reports of pregnancy are available about women with CTGA but atrioventricular valve regurgitation and ventricular dysfunction are recognized important complications in patients with CTGA. As so, appropriate cardiovascular evaluation should be assessed before pregnancy and it is primordial that these pregnancies be closely monitored by a multidisciplinary team that includes obstetrician cardiologist and anesthesiologist.

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Maternal and perinatal outcome in patients with congenital atrial or ventricular septal defect

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Objective: The objective of this study was to evaluate maternal and fetal outcome in patients with congenital atrial (ASD), ventricular (VSD) or atrioventricular septal defect (AVSD), followed in a tertiary-care hospital. Methods: We retrospectively evaluated 27 pregnancies from 23 women. Follow-up data included surgical correction before pregnancy, presence of pulmonary hypertension, occurrence of cardiac and obstetric events, labor data and neonatal outcome. Results: Ten patients had ASD, ten VSD and three DSAV from which six, four and two patients had a corrective surgery before pregnancy, respectively. Seven women had pulmonary hypertension with mean pulmonary artery systolic pressure of 50.4±14.2mmHg and other two had Eisenmenger’s syndrome (ES). Four patients deteriorated during pregnancy or postpartum. One case of hemoptysis, two pulmonary edema (one patient in the second day of puerperium), one acute atrial fibrillation and one maternal death were observed. There were 7 vaginal deliveries, 19 caesarean sections and 1 medical abortion. There were 6 preterm deliveries and 2 small-for-gestational-age newborns. One patient with ES died with 28 weeks and 4 days due to pulmonary thromboembolism and underwent a postmortem caesarean section. Conclusions: Patients with ASD, VSD and AVSD present greater risk of complications, even if the defect was corrected before pregnancy. It is important to follow these women in a tertiary-care hospital. ES is particularly hazardous.

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Successful vaginal delivery of twins after percutaneous balloon valvoplasty during pregnancy in a patient with severe mitral stenosis

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Background: Rheumatic disease is the most common cause of cardiopathy in childbearing women in our country. Mitral valve stenosis increases the morbidity and mortality during pregnancy, leading to congestive heart failure. Percutaneous mitral balloon valvuloplasty is a safe and effective method of improving mitral area, with a low morbidity and mortality rate for the fetus and the mother.

Case Report: A 32-year-old gravida 5 para 4, was diagnosed with severe mitral valve stenosis (mitral valve area=0.7cm²) in the 16th week of a twin pregnancy. Despite of intensive clinical therapy with beta-blockers and diuretics, she remained in functional class IV. A percutaneous balloon valvuloplasty was performed in the 21st week of the pregnancy, with clinical improvement (mitral valve area post valvoplasty=1.7cm², functional class II). She remained treated with propranolol throughout pregnancy. At the 35th week, she had a premature rupture of membrane with subsequent spontaneous labor under caudal analgesia and delivered vaginally (first twin vertex, second breech presentation) without obstetrical or clinical complications.

Conclusion: Percutaneous balloon valvoplasty - when feasible - can improve maternal and fetal prognosis. Vaginal delivery, even in twin pregnancies, can be safely undertaken in patients with heart disease.

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Perinatal outcome in pregnancies of adolescents with heart disease

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Objective: To evaluate maternal and fetal outcomes in pregnant adolescents with heart disease. Methods: We evaluated retrospectively 61 adolescents with heart disease whose deliveries occurred in a tertiary-care hospital. Results: The mean age was 17.5±1.24 years-old. There were 77.1% primigravida and 22.9% multigravida. The heart diseases observed were: arrhythmia (6), cardiomyopathy (6), rheumatic (20) and congenital (29). The mean gestational age at labor was 38±2.9 weeks. We observed caesarean sections in 47.5% and vaginal deliveries in 52.5% of the cases. In the cardiomyopathy group, there were five caesarean sections and one vaginal delivery, in the rheumatic group 6 caesarean sections and 14 vaginal deliveries (p=0.02). Among the patients who had prenatal care into the hospital (HC-FMUSP) 24 were submitted to caesarean sections and 29 to vaginal deliveries, while 5 patients with another type of prenatal care had caesarean sections and 5 vaginal deliveries (p=0.86). The mean newborn weight was 2,791±564g, and 32.8% were small-for-gestational age. This occurrence was observed in two patients with arrhythmia, two with cardiomyopathy, 10 with congenital disease and 6 with rheumatic disease. No difference in birth-weight was detected between the different disease groups. Conclusions: The most frequent heart disease in this group of patients was the congenital disease. The cardiomyopathy group patients underwent more caesarean sections. No differences were observed in perinatal Results.

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CO2 lasertreatment of cervical intraepithelial neoplasia (CIN) and obstetrics outcomes: Report of 270 cases

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Introduction: Treatment of CIN involves ablation or excision of a portion of the cervix. The peak incidence occurs in young women: this might be of significant impact on pregnancy outcomes: increased risk of preterm delivery, pPROM and cervical incompetence is reported.

Clinical findings: In a retrospective study we considered the first singleton pregnancy after treatment in 270 women with a history of cervical laserconization (79 pts) or laservaporization (191 pts). The mean age at treatment was 28.4 years (range 18-41 yrs). We treated 136 LSIL and 134 HSIL. The mean depth of treatment was 8.4mm for laservaporization and 13.7mm for laserconization.

Results: We made 2 therapeutic cerclages for cervical incompetence. There were 5 pPROM in laserconization group (6.3%) and 1 in laservaporization group (0.5%) (p0.013). Threatened preterm labor was detected in 17 women (6.3%); only 3 had spontaneous preterm deliveries. We observed 27 preterm deliveries (10%) before 37 weeks of gestation; only 17 (6.3%) were spontaneous, the other ones were medical inducted. There was a significant difference (p0.02) in preterm delivery rate between laserconization group (12.7%) and laservaporization group (3.7%). We found 20 recurrences of CIN (7.4%) after a median time of 71 months: none was invasive.

Conclusion: In our experience we found a low risk for cervical incompetence, pPROM and preterm delivery in patients treated for CIN. Our data show that CO2 lasertreatment is a safe therapy for cervical pathology assuring to women a low risk of recurrence without interfering with a good outcome of future pregnancies

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Safety of cesarean myomectomy

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Aim: To examine the safety and appropriateness of uterine myomectomy during caesarean section.

Methods: We conducted a retrospective analysis for 73 patients who underwent myomectomy during caesarean section and 69 patients who had uterine myomas, but underwent caesarean section only, between January 2002 and December 2007. Based on the medical records, we conducted an analysis of the characteristics of the uterine myomas, the hematologic changes which occurred between the preoperative and the postoperative phases, the complications, and the lengths of hospital stay.

Results: The changes in the hemoglobin values between the preoperative and postoperative phases, indicating the degree of intraoperative bleeding, were evaluated. There were no significant differences between the two groups (caesarean myomectomy group [0.9±1.3g/dl] vs. control group [1.3±1.3g/dl]). There were also no significant differences in the frequency of blood transfusion, the incidence of postoperative fever, the duration of surgery, and the length of hospital stay between the two groups. In the patients who received a blood transfusion intraoperatively, the increased amount was added to the hemoglobin changes between the preoperative and postoperative phases (the adjusted value). The difference in the adjusted value did not reach statistical significance (caesarean myomectomy group [1.1±1.5g/dl] vs. control group [1.3±1.6g/dl]). When the size of the uterine myoma exceeded 6cm, the operative time was longer in the caesarean myomectomy group.

Conclusions: Cesarean myomectomy is a safe surgical option without significant complications if performed by an experienced obstetrician.

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The course of pregnancy, labor and puerpuerium in women with uterine fibroids

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Introduction: The average age of pregnant women is increasing and thus increases the likelihood of pregnancy coinciding with uterine fibroids. To counsel affected pregnancies properly it is crucial to be aware about complication rates associated with fibroids during pregnancy, in labor and the time of the puerpuerium.

Method: We analyzed 9705 deliveries at a tertiary care centre (Charité University Hospital) between 2001 and 2007.

Results: 96 patients (0.99%) presented with uterine fibroids. The average age was 35.5 years. 79 patients (82.3%) delivered spontaneously at term. In 51.7% the course of the pregnancy was uneventful. The most common complication was lower abdominal pain in 30.2%, which was directly correlated to the fibroids in 11% of the cases, followed by miscarriage in 22.6% and preterm labor in 18.9%. Only 30.8% had an uncomplicated delivery. The caesarean section rate in the fibroid group (61.5%) was significantly higher (p<0.001) compared patients without fibroids delivered during the same time frame. The most common indication for primary caesarean section was mal-presentation in 35.1% of all caesarean sections. Fibroids obstructing the birth canal was an indication in 16.2%. 79.5% of all patients with fibroids had an uneventful course of the puerpuerium. Conclusion: The presence of uterine fibroids does not necessarily indicate a poor prognosis. However, due to the likelihood of complications and the mode of delivery they have to be regarded and treated as high-risk pregnancies which need close supervision and timely planning of the mode of delivery.

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Myomectomy of a large uterine leiomyoma at emergency caesarean section- a case report

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Uterine leiomyomas are present in about 2% of pregnant women. They are responsible for diverse pregnancy complications such as miscarriage, intrauterine growth restriction, pain, necrosis, bleeding, abruptio placentae, premature rupture of membranes (PROM) and complications during and after delivery such as postpartum hemorrhage. Optimal treatment of leiomyomas occurring in pregnancy is controversial.

We report a case of a 38-year-old gravida 6 para 5 who underwent emergency caesarean re-section in 24 weeks of gestation for premature contractions, PROM, strong vaginal bleeding and prolapse of the umbilical cord. Ultrasound examination at admission showed a large leiomyoma in the right part and a vital fetus in the left part of the uterus.

After delivery of a premature vital fetus (564g, Apgar 4/6/7) 13 minutes after admission, inspection of the uterus confirmed a huge intramural leiomyoma of 150x140x80mm. We noted bleeding out of the myoma area, the myoma seemed encapsulated and we anticipated contraction problems. Thus, the myoma was manually enucleated which the surgeon's fingers only. The uterus was closed in several layers. Intra- and postoperative course were without any complications. Histology confirmed a leiomyoma of 840g. The newborn was discharged from hospital on 124\textsuperscript{th} day of life in good condition.

Our case illustrates that dissection of large and single encapsulated myoma during caesarean section is a safe procedure in situations with high risk of atonic bleeding. In addition, enucleation of single encapsulated fibroids during caesarean section could prevent hysterectomy and thus preserves fertility. In our presentation we discuss the current literature.

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Spontaneous anteflexion of an incarcerated uterus upon necrosis of a large myoma in pregnancy

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We present the rare case of a 34 year old primigravid woman with incarcerated uterine leiomyoma. In the patient myomata were known for over two years. Due to intramural position myomectomy was not attempted. Following spontaneous conception, the fundal myoma was showed a diameter of 15cm in 13th gestational weeks. The uterus was in an upright position and the cervix about 40mm. In 16 weeks she presented with increased abdominal pain. The fibroid had retained the uterus in the small pelvis and retroflexio uteri occurred. The cervix was wedged and elongated behind the symphysis pubis with a length of 70mm. Reducing the uterus into the abdominal cavity by placing the patient in knee-chest position failed. In 23 weeks she was admitted again due to increasing abdominal pain. The myoma was completely necrotic. The distance between uterine cavity and capsule was 3.5mm. Lung maturation was induced in 24 and repeated in 29 weeks. Nifedipine tocolysis was administered. In 30 weeks the uterus erected itself spontaneously. Bladder and cervix were in normal anatomic position. Due to the increased risk of uterine rupture caesarean section and enucleation of the tumor with 2.5 liters of necrotic fluid was performed in 35 weeks and a healthy female was born. Leiomyoma occur in 20-40% of women beyond 30-35 years of age and are associated with higher incidence of preterm labor, preterm rupture of the membranes, labor dystocia, uterine rupture, retained placenta, uncontrollable postpartum hemorrhage.

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Cervical prolapse during pregnancy  
(Report of two cases)  

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Objective: The cervical prolapsus is rare during the pregnancy. Less than 245 cases were reported in the literature, and only 5 cases reported after 1968.  

Case Report: This article reports two cervical cases of prolapsus during the second and third trimester of the pregnancy. They had referred with incarcerated the cervical prolapsus in our center. Premature labor occurred all the two women regardless conservative management. A patient developed the sepsis.  

Conclusion: Appropriate management of cervical prolapsus need diagnose of prolapsus pre-pregnancy and conservative management in pregnancy were not always successful.  

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Risk factors, clinical presentation and perinatal outcome of abruptio placentae

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Objectives: To determine the incidence, associated conditions, and pregnancy outcome of abruptio placentae in our institution.

Methods: Retrospective assessment of 116 women with placental abruptio who delivered in our Department between Jan. 2000 and Dec. 2008. Possible risk factors, clinical manifestations and fetal-maternal morbimortality of abruptio placentae were reviewed.

Results: Mean maternal age was 30.7±5 years and 35.3% of them were nulliparous. Associated conditions were cigarette smoking (7.8%), chronic hypertension (7.8%), gestational hypertension (5.2%), pre-eclampsia (10.3%), 1st and 2nd trimester bleeding (20.7%), multiple pregnancy (5.2%), previous caesarean section (15.5%) and placenta previa (9.5%).

The most common manifestations of abruptio placentae were: vaginal bleeding (87.9%), fetal heart rate abnormalities (38.0%), hypertonia (30.2%), bloody amniotic fluid (29.3%) and abdominal pain (8.6%)

Overall, 59.5% of pregnancies had preterm labor and 94.8% were delivered by caesarean section.

A retroplacental blood clot was seen by ultrasound with a sensitivity of 48%. Mean new born weight was 2,241.7±853g. Perinatal death occurred in 0.11 ‰ of all fetuses (8 stillbirths and 5 neonatal deaths).

Admission in the intensive care unit was necessary in 55.2% of the newborns; 16% had IUGR and 12.1% had an Apgar score <7 at 5 minutes.

Maternal anaemia after labor occur in 19.8%.

Conclusions: The main clinical presentations of abruptio placentae were vaginal bleeding and fetal heart rate abnormalities. Abruptio placentae was found to be significantly associated with preterm labor, cigarette smoking, chronic HTA, pre-eclampsia and placenta previa.

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Pregnancy after renal transplantation; 2 Case Reports

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Solid organ transplantation is an alternative treatment for end-stage organ failure during last decades. The rate of pregnancy rises up by the advanced technology in transplantation and new immunosuppressive drugs. The renal and endocrine functions immediately return after transplantation and by the normal sexual activity, the pregnancy rate rises up to 1/50. These pregnancies should be considered as high risk pregnancies and should be managed by a multidisciplinary approach in a tertiary unit. We reported two pregnancies after renal transplantation. They underwent transplantations in our hospital. Our first case was a 29 year woman who had a renal transplantation in 2004 and was given birth by caesarean section in 2007. The second case was a 31 year old woman who had a renal transplantation in 2005 and was given birth by caesarean section in 2008. Both of them underwent caesarean section at term and no malformations were seen in their newborns.

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IVF Pregnancy with previous unilateral nephrectomy. Case Report

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This paper shows a protocol for successful IVF pregnancy at women with previous unilateral nephrectomy.

Methodology: 27 years old patient with unilateral nephrectomy and primary infertility. There was no pregnancy after one year of regular sexual relationship. After doing all necessary tests of the couple I recommend HyCo Sy for the checking the tubes, which where obstructed I recommend IFV as secure way leading to pregnancy. After synchronization of the cycles with contraceptive pills, than blockade of the ovulation we stimulate follicles by using gonadotropins in long term protocol. After ICSI-ET we succeed. CVS was done in 10th week of gestation. Till the delivery she had a monthly control of all vital parameters laboratory and ultrasonography of the baby and kidney by obstetrition urologist and nephrologists.

Result: Patient deliver live healthy baby by SC in 37th GW, BM 3600-54-37, As 9-10.

Discussion: This case shows that younger couples can succeed in fertility even though they had previous hard operation on urogenital tract.

Conclusion: This high-risk pregnancy after nephrectomy and IVF must be controlled multidisciplinary by narrow and comprehended work between perinatologist, urologist and nephrologist.

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Subarachnoid haemorrhage during pregnancy

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41-year old woman in her second pregnancy who, at week 27 of gestation, presents a subarachnoid haemorrhage. During ICU admission neurological disorders are complicated by the presence of a large aneurism of the posterior communicant artery that needs embolization and intraventricular drainage. The evolution and appearance of meticilin resistant staphylococcus aureus in the cerebrospinal fluid advises to finalize the gestation to ensure an optimum control of the neurological and infectious pathology.

An elective caesarean section is carried out.
Antenatal steroid therapy for fetal lung maturation was complete. Newborn male 1000g weight; apgar’s score 6/9.
Afterwards catheter derivation is carried out with a correction in the antibiotic therapy with patient clinical improvement until discharge after two weeks.
The newborn was transferred to an infant surgical unit three days after birth due to an intestinal perforation for which surgical intervention was satisfactorily performed. Recovery was satisfactory with correct weight increase until discharge. No neurological pathology related to prematurity was present.

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Objectives: Triplet pregnancies are at risk for pre-eclampsia and preterm labor during the pregnancy. Aim of the study: The aim of the study is to show 2 patients treated in General Hospital Kumanovo.

Material and methods: History of illnesses and delivery number 1926 and 2723.

Case 1: 31 year old healthy woman. It was her first pregnancy stimulated with clomifen citrate. At 17-th g. w. she had putted on cerclage. During the pregnancy she had normal blood pressure. She was treated with Fe, vitamins and Mg. She got only 15kg till the 35-th g. w. when she was treated for preterm labor. Her blood pressure is still normal, but her platelets are low and her liver enzymes are little bit upper than normal rate. We decided to terminate the pregnancy with C-section in 35, 5 gestational weeks. We had three healthy babies; I was 1680g, II 1710g and III 1900g. Postoperative period and lactation was normal.

Case 2: 33 years old woman with II spontaneously pregnancy. At 18-th g. w. she had putted on cerclage. At 29-th gestational week she was treated for preterm labor. She got 22kg till the 33-th week. She was treated with Fe, vitamins, Mg, plasma and human albumins. At 35-th week she got oedemas, blood pressure was 140/90. She was treated with antihypertensive drugs during 24h. Because of the difficulty with breathing it was preformed emergency C-section. We had three healthy babies; I one was 2200g, II 2100g, III 2350g. Postoperative period was difficult with pulmonary oedema, heart complications.
Early mobilization and leg compression in proximal deep venous thrombosis during pregnancy

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Objective: To evaluate the benefits of compression and walking exercises in comparison with compression and bed rest in the acute stage of proximal deep venous thrombosis (DVT) in pregnant women.

Material and method: Thirty-two consecutive pregnant women with proximal DVT diagnosed by color duplex ultrasound were divided into two groups. Group A consisted of 15 patients who received elastic compression bandages and early mobilization, and group B consisted of 17 patients with compression bandages and bed rest. All patients received heparin therapy. The clinical characteristics of the three groups were comparable. We assessed the reduction of subjective pain daily using a Visual Analogue Scale and the objective pain using Lowenberg test, the reduction of edema was recorded initially and on day 2, 4 and 7. Ultrasound was repeated after seven days.

Results: Resolution of subjective pain was faster during the first three days and near absent at the end of the study period in group A (p<0.001). Objective pain reduced dramatically in group A during the observation period while in group B decreased during the first three days almost by half but remained constantly present over the remaining days (p<0.001). The same was true for the measurement of leg circumference (p<0.05). There was no pulmonary emboli and progression of thrombus diameter.

Conclusion: Pregnant women with proximal deep vein thrombosis may benefit from leg compression and early mobilization for a faster resolution of the signs and symptoms and this method does not constitute an additional risk factor for pulmonary embolism.

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Propranolol and pregnancy

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Propranolol, a non-selective beta-adrenergic blocking agent, has been used for many indications in pregnancy. Apparently not teratogen, continued propranolol and daily doses of 160mg or higher appear to produce more fetal and neonatal side effects including fetal growth restriction, reduced placental weight, hypoglycemia, bradycardia, birth apnea, hyperbilirubinemia. The authors present a pregnant patient with Wolff-Parkinson-White syndrome, suffering recurrent supraventricular paroxystic tachycardia, initially medical treated with propranolol 20mg/day. Increased frequency of episodes required higher propranolol doses (280mg/dl at birth) and occasionally adenosine. Radiofrequency ablation was attempted at 24 week with no success. Ultrasound surveillance indicated progressive decreased of fetal weight: percentile 5.4 at 36 weeks +5d and absent umbilical artery end-diastolic flow associated to blood flow redistribution of medial cerebral artery which anticipated delivery. Male newborn with 2175g, apgar index – 8/10 at 1 and 5 minutes respectively, did not present other complications. As already described in several studies, fetal growth restriction appears to be significantly correlated to chronic, high dosage propranolol therapy, which doesn't apply to others neonatal complications.

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Pregnancy and serious Klippel-Feil syndrome with participation of lung

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The Klippel-Feil syndrome is a disease of cervical spine and serious deformity with reduction of movement. It results from failure of normal segmentation of cervical somites in early gestational age. We know autosomal dominant and recessive forms. In literature worldwide are few cases described. Case report: A 23-year-old primiparous woman (135cm, 32kg) with severe kyphoscoliosis, an immobile cervical spine, short stature, and dyspnoe due to the Klippel-Feil syndrome presents for consultation in 7 weeks of gestation. Pulmonary function test shows obstruction and serious restriction. First hospitalization is necessary because of pneumonia, second with pulmonary infect in 18 weeks of gestation. After that ambulant care is possible until 26 weeks of gestation. Dyspnoe, restlessness and fear leads to hospitalization until labor in 31 weeks of gestation. Because of respiratory decompensation and breech position of the baby delivery by Cesarean section in general anesthesia in the preferred procedure. Development of the baby in pregnancy is normal and the patient is successfully delivered of a healthy girl (birth-weight: 1180g, length: 37.5cm, Apgar 7/8/8, ph 7.33, BE-2.8). The baby lies on neonatal intensive care for 6 weeks until discharge. Conclusion: Intensive support and a high level of interdisciplinary cooperation in high risk pregnancy (Klippel-Feil syndrome) lead to a successful delivery and a healthy newborn.

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Acute pseudo-obstruction of the colon (Ogilvie’s Syndrome) after caesarean section: A rare and serious complication

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We report on one case with Ogilvie syndrome (OS) after caesarean section by a 19-year-old, primiparous women. 72h post operation the patient developed gross abdominal distension, inability to pass flatus and pain in all four quadrants. In the suspicious case of a peritonitis we take the re-laparotomie. The operation-field shows a massive dilatation of the whole colon without obvious cause. A daily colonoscopic decompression is following.

Conclusion: Ogilvie syndrome is a rare and serious complication after caesarean section and other surgical intervention with a mortality rate of 15-20%, when ischemia develops or bowl perforation the rate can be as high as 36-50%. OS is characterized as acute colonic dilatation by a adynamic colon in the absence of obvious colonic disease or mechanical obstruction. Uptill now 23 cases of OS after caesarean section have been described in the literature. It remains unclear how etiology and pathogenesis Result in acute pseudo-obstruction of the colon (APCO), but it has been associated with predisposing factors like intra-abdominal surgery, retroperitoneal trauma, sepsis, viral infections and metabolic imbalance. The pathological cause seems to be disturbance of the autonomic innervation of the colon.

The best documented treatment of APCO is intravenous neostigmine. A colonoscopic decompression is urgent when the cecal distention is 12cm or more. Perforation, ischemia and repeated failure of colonoscopic decompression are indications for surgical intervention.

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Herpes Gestationis – A case report

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Dermatoses of pregnancy includes the skin eruptions that are specifics to pregnant and puerperal woman.
Pemphigoid Gestationis or Herpes Gestationis is characterized by a blistering disease associated with pregnancy and increased fetal risk. It’s incidence is 1/1700 to 1/50000 pregnancies and occurs during the second or third trimester or post partum.
Herpes Gestationis (HP) is the only Dermatoses more clearly defined, because immunofluorescent studies are available to confirm the diagnosis.

The authors present a case of a 31 year-old pregnant woman, who was diagnosis with HG at 29th week of her second pregnancy. The disease presented with pruriginous, erythematos-edematous lesions associated with blisters, localized on the abdomen and superior members. The diagnosis was made by immunofluorescent studies. The patient was treated with corticosteroids with little improvement of the pruritus.
She delivered at 36 week a girl with normal apgar score and with no evidence of disease.

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Pregnancy in patients with Cystic Fibrosis - a case series

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Cystic fibrosis (CF) is one of the most common autosomal recessive inherited diseases amongst Caucasians. The severity of clinical disease varies with the extend and the degree of involvement of the various organ systems in the pregnant and non-pregnant female with CF. Although there is a wide spectrum of clinical manifestations in CF, the progressive bronchopulmonary disease is the predominant cause of morbidity and mortality in CF. Pancreatic involvement with progressive exocrine pancreatic insufficiency eventually leading to Diabetes as well as maldigestion associated with malabsorption are common problems. With the dramatic increase in survival of patients with CF during the past few decades associated with an improvement in therapeutic modalities, a rise in pregnancy-rates has been observed amongst affected women. Both maternal morbidity and mortality are increased with impairment in pulmonary function being the most common complication. Fetal complications consist mainly of Growth Restriction and of an increased prematurity rate to about 25%. In order to evaluate the impact of CF on fetal and maternal health, we performed a retrospective analysis on 11 pregnancies in 11 CF patients cared for by a multidisciplinary team in our unit. Nine healthy infants were delivered, one of them prior to 32 weeks. Women with a better health statue prior to starting pregnancy were more inclined to successfully complete a pregnancy.

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Multiple Sclerosis and pregnancy

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Introduction: Multiple sclerosis (MS) is an autoimmune condition occurring more frequently in childbearing women, in which the immune system attacks the central nervous system, leading to demyelination.

Objective: To evaluate impacts between MS and pregnancy.

Patients & Methods: This is a retrospective study of 9 pregnancies in 8 women followed at our centre between 2004 and 2008. The evaluated variables were: form of presentation and duration of the disease, evolution during pregnancy, medications, obstetric complications, type of delivery, neonatal outcomes and lactation.

Results: Seven women had exacerbation-remission form of MS and one had progressive form. Mean duration of disease before pregnancy was 9 years. Six women did not take medication for MS during pregnancy and 2 had to interrupt it because of potential teratogenic effect. MS worsened in 3 cases. Eight pregnancies had good evolution with delivery at term (one first trimester miscarriage occurred). Six caesareans were performed, 3 of which resulted from severe maternal disease. No case of low birth weight or neonatal asfixia was found; however, there were one case of neonatal sepsis and one of neonatal jaundice with poor ponderal progression. Lactation was encouraged in all cases, though three women had to interrupt it because of worsening of MS.

Conclusion: Planning of pregnancy was deficient (two women had to interrupt dangerous medication abruptly). The global prognosis of pregnancy and newborns was good in our study, nevertheless, a greater number of cases is needed to obtain more conclusive Results.

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Stroke: a catastrophic event during pregnancy and the puerperium

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Objective: Study the prognosis of stroke (considering separately brain ischemia and brain haemorrhage) in pregnancy and the puerperium.

Materials and Methods: Review of the cases of stroke during pregnancy and puerperium that occurred in our hospital between 1995-2005.

Results: We found 13 cases of stroke, four cases (31%) occurred during pregnancy and 9 cases (69%) during the puerperium. Six cases corresponded to brain haemorrhage and seven cases to brain ischemia. Within the 6 cases of brain haemorrhage we found 3 deaths (50% mortality). Five of these patients needed assessment in intensive care unit (ICU) with a mean stage of 20 days (median of 8.5 days). Those who survived showed no disability. Brain ischemia caused no deaths among our patients, and only one patient needed admission in ICU with a stage of 4 days. Six out of seven patients (85.7%) showed persistent disability.

Conclusions: Brain haemorrhage was associated with a higher mortality while brain ischemia was associated with a higher neurologic disability

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Vegetative status of infants born from mothers with neurocirculatory asthenia

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Vascular tone regulation disorders in neurocirculatory asthenia (NCA) in pregnancy significantly increase risk of pathological course of pregnancy and adversely affect fetus development that Result in perinatal mortality and morbidity. 120 pregnant women with NCA were studied: 55 (45.8%) women had hypertonic, 47 (39.2%) - hypotonic and 18 (15%) cardial form. 20 healthy pregnant women and their infants were controls. The newborns were examined by Apgar score after delivery. Vegetative tone of newborns was studied clinically on the 1st and 3rd day after delivery. Vegetative nervous system was evaluated by its baseline tone and reactivity. Vegetative tone was studied by cardiointervalography, vegetative reactivity by the Results of orthostatic and immunostatic test with ECG recordings, blood pressure and Ashner test. The analysis of delivery outcomes showed that regardless of maternal NCA form, infants were born with some degree of asphyxia more frequently by 2.3 times than in healthy pregnant women. In neonatal adaptation in maternal NCA newborns, various disadaptation syndroms were developed, including most common vegetative disorders: mottled skin, acrocyanosis, thermolability, saliva hypersecretion, vomiting, respiratory and heart rate disorders. In 15% newborns normotonia, in 37.5% sympathicotonia, in 32.5% vagotonia were diagnosed. Hypersympathicotonia observed in 6 (5%) infants was accompanied with pupillary widening, decrease in heart rate, mucus hypersecretion that required frequent sanation of upper respiratory tract, as well as increase of gastric peristalsis. The most expressed signs of vegetative dysfunction was in infants born from mothers with hypertonic NCA that Result in complicated and long period of neonatal adaptation.

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Chronological changes in recognition rate and prevalence of premenstrual syndrome in female university students

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It is generally believed that the spread of medical knowledge leads to health promotion in perinatal medicine. The rapid spread of the Internet may also play important roles in health promotion, especially those in their teens and twenties. However, changes caused by the effects of such a spread of medical knowledge in women's health have seldom been studied. In this study, we investigated chronological changes in young women's knowledge of premenstrual syndrome (PMS). We carried out a questionnaire survey regarding the recognition and severity of symptoms of PMS in female university students (present study: n=314) (mean: 20.6 years old). We used the same questionnaires that we employed four years ago (previous study: n=339) in the same universities. Initially, we assessed the recognition rates of PMS after showing subjects a definition of PMS by the Japan Society of Obstetrics and Gynecology, and the rates were 37.2 and 29.7% in present and previous studies, respectively. Regarding the prevalence of PMS, 59.3 and 23.2% of subjects replied that they had self-awareness of PMS in the present and previous study, respectively. Particularly, the prevalence of breast tenderness, irritability, sleeplessness, overeating and changes in food tastes increased. A Google Japan search using the keyword "PMS" revealed that the number of hits in 2007 increased by 3.7 times compared to that in 2003, although hits for "dysmenorrhea" increased by only 2.5 times. These results suggested that the spread of information on PMS might be related to an increase in its prevalence.

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Episodic angioedema associated with eosinophilia and pregnancy: A case report

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Episodic angioedema associated with eosinophilia (EAE) is a rare disease, which is characterized by recurrent angioedema, urticaria, fever, and markedly high level of eosinophilia. Many reports of EAE are available, but there are few reports that refer to pregnancy with EAE. We here present a case of EAE associated with pregnancy.

The patient was a 36-year-old Japanese woman in her first pregnancy. She had been diagnosed as EAE when she was 20 years old, then she had been cared for at the Department of Internal Medicine in our hospital. She had taken a turn for worse every two or three menstrual periods and had treated with prednisolone and furosemide. She conceived spontaneously and came to our department. We had carefully checked her physical condition and her laboratory data. During her period of pregnancy, she had sometimes developed a fever, but with the exception of fever, other troubles had not been found and her pregnant course was fair. At 41 weeks of gestation, she spontaneously delivered a female baby vaginally. Both the mother and the infant were discharged without complication.

EAE is uncommon disease, and it is still unknown how EAE would affect pregnancy or how pregnancy would affect EAE. Some patients of EAE are young, and they may want to conceive and have a child. This case report suggests there are some possibilities for EAE.

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Severe case of puerperal psychosis treated by successful electroconvulsive therapy – Case report

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Introduction: Puerperal psychosis is an uncommon but serious disorder, involving both fetal and maternal risks. It usually occurs up to 1 month after delivery. Patients present with frank psychosis, cognitive impairment and severely disorganized behavior, in stark contrast with previous functioning. Risk factors have been identified, but no clear precipitant is known. Rapid and accurate diagnosis and treatment is essential. There is a general belief that electroconvulsive therapy (ECT) is effective in treating severe or treatment-refractory postpartum affective illnesses, but evidence to support this assertion is lacking.

Case Report: We present the case of a healthy 28 year old woman who had a normal pregnancy with a term delivery. The early puerperium was uneventful. Three weeks after delivery she suddenly initiated a clinical picture of severe puerperal psychosis. After various unsuccessful antipsychotic therapies, ECT under general anesthesia was decided. Clinical recovery was prompt and dramatic. At one-year follow-up, the patient is well, without any medication, although mentioning a slight memory deficit.

Conclusions: It is fundamental to be alert to postpartum affective illnesses. ECT can be an excellent choice for women who have failed prior medication trials.

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A 8cm separation of symphysis pubis during vaginal delivery

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Background: Symphysis pubis separation during the vaginal delivery is rare but severe complication. Case: A 30 years old primigravida admitted to hospital for pitocin induction at 40 weeks gestation. Uterine cervix was fully dilatated in 6 hour 30 minute later after induction. The physician heard a loud pop while she was in the vigorous labor at 2nd stage and then within 45 minute of 2nd stage, she delivered a healthy 3,700gm boy. From immediate postpartum, the patient complain of severe back pain and iliosacral pain and she was observed suprapubic edema and tenderness. She was unable to stand or walk without assistant. In spite of analgesics, she complained of severe back pain continuously without symptom improvement. Physical examination at that time was for back pain and suprapubic tenderness. Postpartum 5 day, a pelvic x-ray revealed a 8cm separation of symphysis pubis. The orthopedic surgery department was consulted. The patient was applied pelvic sling (Hammock traction) with spine position for 1 week. After 1 week, the gap of symphysis pubis was decreased to 3cm and then she was fitted with a pelvic brace. She required postpartum hospitalization for 28 days. Due to severe pelvic pain, She was readmission on postpartum 36 days and 1 week later after discharge. She was followed up by OPD at present.

Conclusion: Although there some controversies, severe symphyseal separation during vaginal delivery can be managed without surgery and in postpartum pain on symphysis, pelvis radiograph study is necessary for exclusion of symphysis pubis separation.

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MEN 1 syndrome associated with pregnancy

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Introduction: Multiple endocrine neoplasia type 1 (MEN1) is an autosomal dominant predisposition defined by the presence of two of three main tumors (parathyroid, entero-pancreatic endocrine and pituitary adenomas). Insulinomas are rare insulin-secreting tumors with an incidence of 1 in 250,000/year. In MEN1 syndrome they are frequently small, may be multiple, benign or malignant. Malignancy or association with MEN1 is verified in less than 10-15%. To our knowledge, no more than 25 cases of insulinomas associated with pregnancy have been reported.

Case Report: We present a 33 year-old primigravida, with history of MEN1 syndrome (with previous partial pancreatectomy and ganglion excision due to malignant insulinoma and parathyroidectomy due to primary hyperparathyroidism with parathyroid adenoma). The tumors’ aggressive character, allied by the multiple foci scattered on the surgical specimen held back the clinicians in allowing a pregnancy to take place. However, and before knowing the Results on the follow-up CT scan, she appeared pregnant of 8 weeks. The scan revealed local recurrence. Under informed consent, and according to the multidisciplinary groups’ decision, pregnancy was terminated at 10 weeks.

Discussion: Malignant insulinomas are rare, therefore few data is available, namely on clinical presentation and long-term prognosis. Although some patients have a prolonged survival, they sometimes have to be submitted to extended surgery, medical therapy and/or chemotherapy. The tumors’ aggressive character, the anatomopathological exam and the local recurrence after primary surgical procedure, supported the decision to terminate pregnancy, in order to clarify, stage clinical situation and define adequate treatment.

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Ulcerative colitis presenting in pregnancy

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Introduction: Ulcerative colitis is a disease confined to the colon in an age from 20 to 40 years mainly. Generally fertility and pregnancy are not disturbed.

Case report: A 31-year-old female patient, in her 29th week of pregnancy, was admitted to our department with complaints of abdominal pain and bloody diarrhea, since 4 weeks before the admission. She had no relevant past history. As the left colonoscopic examination of the patient showed ulcerative colitis, she started treatment with mesalazine (1g/day, in 3 equal doses) and prednisolone (40mg/day). There was a relief in complaints of the patient. At 38th week of pregnancy, she delivered a baby of 2.6kg by caesarean section.

Conclusion: Our experience showed that a diagnosis of ulcerative colitis during the pregnancy can be difficult and an intensive medical therapy did not impair either the course of the pregnancy or the fetal outcome.

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Pemphigus vulgaris during pregnancy – a case report of successful outcome

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Pemphigus vulgaris is an uncommon, immune-mediated bullous dermatosis, which during its active phase is associated with infertility. Pemphigus vulgaris during pregnancy is exceedingly rare – with fewer than 40 cases documented in the literature. The disease may be associated with adverse neonatal outcome, including transient skin lesion, prematurity and fetal death. The recommendation about the delivery is vaginal to minimize skin trauma.

We reported a patient who conceived with this rare disease, required corticosteroids to control the disease and was delivered at term vaginally after the recommendations.

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History of caesarean throughout centuries

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Aim: It comes from the Latin word caedere (cut/intersect). It would be pleonasm then to add the word section “tomoidal cut/section”. With the present study we would like to present an ld but at the same time contemporary obstetric operation.

Material-Method: After the collection of data from passages of the antiquity, the tracing back in historical sources and the choice of the material cautious reading and analysis followed.

Results: There is reference on the caesarean in the Persians (performed in difficult deliveries) and in Hindu (performed posthumously). Buddha was born from his mother rib, Brahma from her navel/umbilical (patterns of caesarean in Egyptians (depictions) and in Chinese (timberwork). Jewish use the caesarean not only in alive but in dead women too). The Incas and Aztecs describe it as following: cutting of the abdominal wall and the uterus, delivery of newborn, manner of hemostasis, stitching of the walls. In mythology, Dionysos, Athena and Asklipius were all born with a pattern/form of caesarean. In Romans, lex Regia, forbade the burial of a pregnant woman and commanded the opening of the abdomen and deliverance/release of the baby. Julius Caesar was named as such because he was born with a caesarean. Under the impact of christianism the appeal to the posthumous caesarean is expanded. In 1500s caesarean was successfully practiced/performed/applied in an alive woman. However, three centuries later the method got to be considered as lethal due to the high levels of mortality. A union against it, was created and the operation was therefore restricted. We have reference from books/readings of Al. Benedetti (1525), Ch. Estienne (1545), Rossetus (1581), Sc. Mercurio (1615), J. Scultes (1653), J. Trauntmann (1670), Th. Bartholinius (1670), W. Smellie (1750) and many others. Amendment of the method by E. Porro (1876) reduced the levels of mortality from 75% to 25%. In 1880 the contribution of antisepsis allowed for its progress, its amendment (1920) and its spread. The use of the antibiotics minimized the danger for post operating infection.

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A common minimum guideline on antenatal care for multinational use

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Objectives: Analyzing the differences and similarities of the national guidelines on antenatal care of the member states of the European Union (EU). Developing a model for integrating existing guidelines to a common minimum guideline to complement national health policies. Definition of the content of such a guideline.

Materials and Methods: Ministries of Health and societies of obstetricians and midwives were asked to fill in a questionnaire on their national guidelines for antenatal care. Descriptive analyzes identified which and how many states recommend a test and to how many people this applied. The tests which were recommended by more than 50% of the states and applied to more than 50% of the inhabitants of the EU were compared to the measures supported by scientific evidence.

Results: All 25 member states of the EU returned a completed questionnaire. 20 of them have a national guideline. 47 tests were reported and 23 of these are recommended for routine care by more than 50% of the states and apply to more than 50% of inhabitants. Those tests are the same as those supported by scientific evidence.

Conclusions: It could be demonstrated for the first time that extracting from national guidelines the measures which are recommended by the majority of states and apply to the majority of inhabitants of the EU leads to a guideline compatible with scientific evidence. Based on this, a common minimum guideline for antenatal care in the EU is recommended.

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The use of PR interval - fetal heart rate correlation analysis in intrapartum fetal monitoring: a case-control study

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Background: Since the introduction of continuous electronic monitoring has not benefited neonatal outcome and led to increased intervention rates, new methods for fetal surveillance have been investigated. Research into fetal electrocardiogram waveform changes has focused on morphologic features (T/QRS complex) and time interval (PR interval) changes. Time interval changes are robust measurements thought to be especially useful when the fetal electrocardiogram is obtained from electrodes on the maternal abdomen. We aimed to assess the diagnostic value of the PR interval – fetal heart rate correlation analysis.

Methods: A case-control study was performed studying the PR interval – FHR relation in 8 fetuses with umbilical artery pH<7.05 and 10 fetuses with umbilical artery pH >7.20 at delivery. The conduction index was determined by correlating PR intervals and FHR with Pearson’s correlation coefficient. The ratio index was calculated using the standard deviate transform. Differences between groups were subjected to statistical analysis. Furthermore, the last 30 minutes of labor were compared with a baseline state, defined as the 30 minutes of data obtained two hours before delivery.

Results: The mean ratio indices were 2.67 (range 1.32-4.48) for cases and 2.12 (range 0.00-4.01) for controls (p=0.308). The conduction indices showed short-term fluctuations from negative to positive in both groups.

Discussion: The absence of significant differences could be explained by the small number of fetal electrocardiogram waveforms available for analysis due to averaging techniques used by STAN. Beat-to-beat analysis could overcome this limitation.

Conclusion: Results show no significant differences between cases and controls.

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Effects of spontaneous and induced labor in presence of normal fetal heart rate patterns on intrapartum fetal oxygenation and perinatal outcomes

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Objective: To compare the values of arterial fetal oxygen saturation (SpO2) and the perinatal outcomes on spontaneous and induced labor in presence of normal fetal heart rate (FHR) patterns. Material and methods: A retrospective research, with 264 pregnant women who presented normal FHR patterns, was done. During labor, they were also monitoring by fetal pulse oximetry. Two groups were obtained according to the way of the beginning of the labor: The group I (n:127) and the group II (n:137) were performed by pregnant women with spontaneous and induced labor respectively. Results: The initial value of SpO2 was 46.24±10.61 in the group I and 45.64±8.51 in the group II (p=n. s.). There were not statistical differences between both groups in the next variables: the average value of SpO2 (47.22±7.08 vs. 46.36±7.78); the minimum value (33.42±10.21 vs. 34.36±10.93) and the maximum value (59.43±6.33 vs. 58.46±7.29).

The total duration of the fetal pulse oximetry was about 162.32±111.03 minutes (min) in the group I and 201.93±131.22 min in the group II (p<0.001). There were not statistical differences in the apgar scoring and in vein ph. However, there was a significant decrease of the arterial pH and a significant increase of the weight in spontaneous labor. Conclusions: The way of the beginning of the labor (spontaneous or induced) does not have any impact on the fetal oxygen saturation. We must analyze if the absence of differences is kept when we include the duration of labor as an intrapartum variable.

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Long term non-invasive fetal electrocardiogram (fECG) and doppler cardiotocogram (CTG) ultrasound during 1st and 2nd stage of labor

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Objective: The objective of the study was to test the reliability and accuracy of non-invasive fetal ECG in comparison to the Doppler CTG ultrasound during first and second stage of labor.

STUDY DESIGN: This was a prospective observational study of a non-invasive fetal ECG using 5 abdominally sited electrodes and one Doppler ultrasound probe of 27 patients. Data were analyzed using the Pearson correlation coefficient, percentage root mean square difference (PRD) and Bland Altman plots.

Results: The success rates during the first stage of labor had a median of 94% (range 25% - 99.9%); the corresponding simultaneous Doppler CTG had a median of 91% (range 75%- 99%) with a median Pearson Correlation Coefficient of 0.85 (range 0.45-0.98, p-value<0.001). During second stage of labor a median success rates of 79.8% (range 8.1%-97.8%) was detected; the corresponding simultaneous Doppler CTG had a median of 91% (range 69.2%-97.4%) with a median Pearson Correlation Coefficient of 0.63 (range -0.16-0.91, p-value<0.001). fECG was detected in 27/27 (100%) patients and a median recording length of 2 hours and 51 minutes was monitored.

Conclusion: This non-invasive fetal ECG presents an alternative reliable and accurate assessment for fetal well-being during labor.

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Evaluation of uterine contraction effect on fetal heart rate

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Introduction: Fetal heart rate monitoring has been introduced since about fifty years ago. Nonstress test is a noninvasive method used to evaluate fetal well-being. Regarding to the fact that uterine contractions are important events during labor phase, this study was planned to determine possible effects of uterine contractions on fetal heart rate tracing.

Methods: 60 term pregnant women who admitted for termination of pregnancy, included in this study. AT first primary Nonstress test was performed, second CTG was traced after active uterine contractions. Each patient was a control case for herself. All possible changes in the Results of CTG were statistically analyzed.

Results: Out of 60 term pregnant women, 51(85%) patients reported acceleration for primary Nonstress test. After uterine contractions, acceleration was seen in 46(76.7%) patients. There was no deceleration on primary Nonstress test. However, deceleration reported after uterine contractions in five (8.3%) cases. 56(93.3%) patients showed FHR variability in primary Nonstress test; variability following the uterine contractions was seen in 58(96.7%). None of them were statistically significant (P value>0.05). Median fetal heart rate baseline in primary Nonstrees test was (141±9.35), this was (140.5±10.5) following uterine contractions. Baseline fetal heart rate reduction, statistically significant, was seen following uterine contraction (R=0.28, N=60, Pvalue=0.02).

Conclusion: uterine contractions does not alter significant changes on FHR variability acceleration and deceleration so observation of any differences on baseline variability, acceleration and deceleration in CTG, after uterine contractions, will necessitate searching for other possible causes.

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Wavelet analysis of fetal heart rate

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The aim is to investigate the diagnostic significant of FHR gain-frequency characteristics for antepartum asphyxia prediction.

The data set consists of 250 CTGs with mean duration 18 (CI95% 17 - 19) minutes. There were two groups of CTGs: the first — 61 CTG are obtained before intrauterine deaths and the second — 189 CTG are obtained in cases of normal perinatal outcome. The data are decomposed by Haar wavelets to get maximum range, standard deviation and mean absolute deviation of fluctuation amplitude in 8 frequency bands.

Logistic regression is used. Diagnostic model is created by analyzing data of 40 CTGs (training sample, 20 CTGs of the first group and 20 CTGs of the second one) without accelerations, decelerations, with mean oscillation amplitude from 3 to 5 beats/minute. Effectiveness of model is checked by analyzing data of the rest 210 CTGs (examination sample).

The mean absolute deviation in fluctuation amplitude within the range of 0.15-0.3 Hz and standard deviation in fluctuation amplitude in the range >0.3 Hz are included into the model (p<0.05). Diagnostic efficacy for CTGs training sample was 90% (CI95%=76 - 97%), sensitivity and specificity were 90% (90%, CI95%=68 - 99%).

Using by wavelet lets to get more effective diagnostic model for estimation of fetal condition by cardiotocography. The application of the model gives the correct Result in 73% (CI95%=60 - 87%) obtained before intrauterine deaths and in 94% (CI95%=89 - 97%) in cases of normal perinatal outcome.

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Perinatal Results in cases of non reassuring fetal status monitored with STAN-21

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Objective: Thanks to methods of fetal intrapartum monitoring such as fetal electrocardiogram analysis (STAN-21), it has been possible to reduce the operative interventions on the labor due to non reassuring fetal status (NRFS), by false positive Results in Electronic Fetal Heart rate monitoring (FHR). The main objective in our study was to analyze the neonatal Results and the intereventions in labors monitored by STAN-21.

Material and methods: A descriptive pilot study in which 80 pregnant women with a single fetus, that in the active stage of labor show a non-reassuring FHR. The women were monitorized with STAN-21. The neonatal Results and the end of labor were analyzed.

Results: The ending of these labors were: spontaneous in 28 cases (35%), and the others in an operative delivery: 25 cases caesarean (31.25%) and 27 cases vaginal (33.75%). The NRFS was the cause of 16 caesarean (64%) and 18 assisted vaginal delivery (66.67%).

In relation to the neonatal Results, the weight average of the newborn was 3,101+/-475.71g. the pH arterial value was 7.31 and the venous pH 7.34. No cases under 7.05.

36 cases (45%) had irregularities in the STAN, which were two-phases ST in the main, 20 (55.56%) and within these, the more frequent were two-phase ST 1 and 2 sporadic.

Conclusions: It has been informed that the monitoring by STAN can reduce the operative deliveries by non-reassuring FHR. In the analyzed cases, we obtain newborns without dangerous acidosis, although we had a high rate of caesarean.

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**Beat to Beat Fetal heart rate variability during pregnancy and labor using non-invasive fetal ECG**

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Objective: The objective of the study was the examination of fetal heart rate variability measures during pregnancy and labor using non-invasive fetal ECG.

Study Design: This was a retrospective observational study of a non-invasive fetal ECG using 5 abdominally sited electrodes (via the Monica AN24) of 68 patients. Data were analyzed in 5 minute epochs only when at least 500 fetal heart beats were identified for data integrity purposes. The evaluation of fetal heart rate measures were either based on beat-to-beat-intervals using standard deviation (SD) and root mean square of successive differences (RMSSD) or based on 3.75 s time intervals using the short time variation (STV) of Dawes/Redman.

Results: Antenatally SD and STV correlate weakly with gestational weeks (r=0.66 and 0.59), whereas RMSSD shows no correlation (r=0.03). The inclusion of sub partum further reduces the correlation in both cases. With regards to CTI antenatally a weak correlation was found with SD (r=0.63), a stronger correlation with STV (r=0.73). Most importantly there was limited correlation between RMSSD and STV (r=0.54).

Conclusion: The beat to beat generated by the Monica AN24 allows true beat to beat analysis. It should be noted that the Doppler CTG only produces a 3.75 second average fetal heart rate and does not allow true beat to beat analysis. Hence the Doppler CTG is highly inappropriate for such measurements. The clinical importance of these beat to beat parameters for fetal assessment is the subject of further studies.

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Prognosis of fetuses with congenital heart disease evaluated by autonomic nerve activities using heart rate variability analyzes involving magnetocardiography

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Heart rate variability (HRV) assessed by electrocardiograms has been widely studied in adult cardiology. However, HRV has been seldom studied in fetuses due to the difficulty in fetal electrocardiogram recording and low resolution of the time domain in echocardiography. Recently, the development of a fetal magnetocardiogram (FMCG) with high resolution of the time domain has enabled HRV analyzes in fetuses. We performed HRV analyzes of FMCG, evaluated fetal autonomic nervous system activities, and studied the association with the prognosis of fetuses with congenital heart disease (CHD). Fourteen normal and 22 CHD fetuses were included in this study. We measured fetal HRV using a 64-ch MCG system, and performed spectral analyzes of HRV. We obtained the total power of spectrums of between 0.04- and 0.15-Hz components (LF), and between 0.15- and 0.4-Hz components (HF), and calculated the ratio of LF to HF (LF/HF). With the advance of gestation in normal fetuses, the LF/HF ratio, well correlated with sympathetic nerve activities, decreased slightly, although the HF, well correlated with parasympathetic nerve activities, increased. In two cases of CHD fetuses, pulmonary stenosis and double outlets of the right ventricle, HF and LF/HF values deviated largely from the standards obtained from normal fetuses, and they died within 24 hours after birth. Our Results suggest that large deviations in the HF and LF/HF of HRV obtained using FMCG might predict a poor prognosis in fetuses.

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Pathological intrapartum pulse oximetry values in fetuses showing variable fetal heart rate decelerations

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Objectives: To compare the frequency of intrapartum values of arterial fetal oxygen saturation (FSpO2) below 30% in presence of normal fetal heart rate (FHR) patterns and variable decelerations (VD) patterns.

Material and Methods: We took a nonprobabilistic sampling of consecutive cases. The study included 264 pregnant women who presented normal FHR patterns and 270 with VD patterns that were also divided into 170 typical VD and 100 atypical ones.

In both groups the FSpO2 was quantified in three categories: FSpO2<10%, FSpO210-19%, FSpO2 20-30%. Four groups were compared according to the type of VD: 1. Normal FHR vs. VD; 2. Normal FHR vs. typical VD; 3. Normal FHR vs. atypical VD; 4. Typical VD and atypical VD.

Results: There was not a statistically difference in the frequency of fetuses with FSpO2<10% and FSpO2 10-19%. In the first of the three groups there was a significant increase of the number of fetuses who had FSpO2 20-30% and presented typical VD: group 1 (24.62% vs. 57%; p<0.001); group 2 (24.62% vs. 55%; p<0.001); group 3 (24.62% vs. 58.8%; p<0.001). However, in the group 4 there weren't statistically differences in any analyzed categories.

Conclusion: The presence of variable decelerations implies an increase in the frequency of periods with slight decrease of fetal oxigenation; no clinical repercussion can be attributed to this fact. More relevant is the fact that the presence of atypia criteria does not imply changes in fetal oxigenation, not therefore giving a worse prognosis.

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Predictive value of pulse oximetry for the development of fetal acidosis

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Aims: To determine the predictive value of fetal pulse oximetry (FPO) for the development of fetal acidosis in cases of non-reassuring fetal heart rate (FHR).

Methods: In a prospective observational study, pulse oximetry monitoring was examined in cases of non-reassuring FHR during single cephalic delivery at 36-42 weeks gestation. The study examined whether FSpO2 values <30% for at least 10 minutes during the last 60 minutes before delivery increase the risk of fetal acidosis. The predictive reliability of this algorithm and the correlation to fetal acidosis (umbilical artery pH<7.15) were analyzed by statistical methods (Fischer exact test and the spearman correlation).

Results: The study included 101 patients with non-reassuring FHR during delivery. The incidence of fetal acidosis was significantly higher when FSpO2 values <30% were recorded for at least 10 minutes (p=0.0). An umbilical artery pH<7.15 was reliably excluded with a negative predictive value of 98.7% and detected with a sensitivity of 92.9%.

Conclusions: A low pulse oximetry oxygen saturation <30% for at least 10 minutes correlates highly with fetal acidosis in cases of non-reassuring FHR. FPO reliably excludes moderate to advanced acidosis and can reduce the frequency of FBA in cases of non-reassuring cardiotocography (CTG).

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Use of the Monica AN 24 maternal-fetal monitor during labor

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The Monica AN 24 maternal-fetal monitor is a pocket size device to record electrophysiological data from the maternal abdomen. With advanced technology fetal and maternal heart rate, maternal movement and uterine activity can be detected. The data can be recorded or transmitted to a display via Bluetooth®.

Since the device currently is only approved for antenatal diagnostics, we have evaluated the usability of the device during labor.

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Does internal tocodynamometry improve the outcome of labour?
A randomised, multicentre trial comparing monitoring of contractions with an intra uterine pressure catheter to an external tocotransducer during induced or augmented labour

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Background Internal tocodynamometry (IT) is, compared to external monitoring (ET), thought to allow a more accurate assessment of uterine activity during labour and thus a more precise titration of oxytocin, and is supposed to result in less instrumental deliveries and less foetal distress. However, there is limited evidence in literature whether this hypothesis is true.

Methods We performed a multicentre randomised controlled trial between 2004 and 2007 in six hospitals in The Netherlands. Women in whom labour was induced or augmented with intravenous oxytocin were randomised to monitor uterine activity by IT or ET. The primary outcome was the number of instrumental deliveries, i.e. Caesarean sections and instrumental vaginal delivery. Adverse neonatal outcome was a secondary outcome defined as a composite variable: Apgar score at 5 minutes <7, umbilical artery pH<7.05 or neonatal admission longer than 48 hours. Analysis was done according to intention to treat.

Results We randomised 1456 women, of whom 734 were allocated to IT and 722 were allocated to ET. The overall instrumental delivery rate was 31.3% in the IT group and 29.6% in the ET group (relative risk (RR) =1.1, 95% confidence interval (CI) 0.91 to 1.2). Composite adverse neonatal outcome occurred in 105 (14.3 %) deliveries in the IT group and in 108 (15 %) deliveries in the ET group (RR=0.95, 95% CI 0.74 to 1.2).

Conclusion There is no evidence that use of internal tocodynamometry during induced or augmented labour improves neonatal or maternal outcome. (trialregister.nl, Id: ISRCTN 52897947)

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Effect of delayed umbilical cord clamping in blood gas analysis (BGA)

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Background: Nowadays, after delivery, the newborn is placed over its mother and the umbilical cord is not clamped until the umbilical cord stops beating. This may report benefits to the newborn. However, this might vary the BGA levels in umbilical cord, which are the most objective determination of the fetal metabolic condition at the moment of birth.

Objective: Study the variations on BGA in umbilical cord associated with delayed clamping.

Materials and Methods: We took 77 pairs of blood samples immediately after the expulsion of the fetus and after clamping the umbilical cord, after it stopped beating. We introduced it in a blood gas analyzer (Radiometer ABL 800 FLEX) obtaining the levels of pH, pCO2, pO2, total Hb, sO2, base excess (BE), HCO3-, cO2, glucose and lactate.

Results: The levels of the different parameters associate among themselves within a range of r 0.65-0.95 (p<0.001). The pre-post clamping differences were statistically significant except for the levels of O2, Hb and base excess (BE).

Clamping deteriorates the levels of pH, pCO2, glucose, lactate and HCO3-. The time between the two samples is associated with pH (r=30; p<0.05) and lactate (r=44; p<0.01), which means that as time passes lactate gets higher and pH lower.

These Results are similar in both arterial and venous analysis.

Conclusions: Delayed clamping of the umbilical cord is associated to a tendency to acidosis, which is a function of time.

Normal BGA patterns will have to be defined in case this procedure becomes a care standard.

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Potential correlation of calcium levels in the amniotic fluid during 15-22 weeks of gestation and pregnancy outcome


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Purpose: To investigate a potential correlation between the levels of calcium concentration in the amniotic fluid during the 15-22 weeks of gestation and the outcome of pregnancy.

Materials and Method: This was a prospective trial in which amniocentesis was performed in 216 healthy pregnant women during the 15-22 weeks of gestation, for prenatal examination. During the examination, the level of calcium in the amniotic fluid was assessed. The above-mentioned pregnant women were followed up and they delivered in our Department. The level of calcium was correlated with the birth weight, the duration of labor and the mode of delivery.

Results: The level of calcium was between 5.0 and 11.6 µg/Dl (mean: 8.1 µg/dL). In 28 cases of premature labor (<37 weeks) there was a direct correlation with raised calcium levels (9.1-11.6µg/dL). No relation between the calcium level and either the birth weight or the mode of delivery could be established.

Conclusions: This study shows that there may be a correlation between high calcium concentration in the amniotic fluid during the second trimester of gestation and the duration of pregnancy that needs further investigation. There was no correlation with either the birth weight or the mode of delivery.

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Umbilical cord lactate levels. Concordance with other parameters in the blood gas analysis (BGA)

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Objective: Study the lactate levels in the umbilical cord and its relationship with other BGA parameters.

Materials and Methods: After the expulsion of the fetus and after clamp of the umbilical cord we obtained 208 samples of 1mL of blood. We introduced it in a blood gas analyzer (Radiometer ABL 800 FLEX) obtaining the levels of pH, pCO2, pO2, total Hb, sO2, base excess (BE), HCO3-, cO2, glucose and lactate.

Results: There is a negative significant association between lactate and pH (r=0.74; p<0.001). Lactate has a closer relationship than pH with BE, HCO3- and glucose. PH shows to be more related to the blood gases.

Conclusions: Lactate seems to be a parameter capable of showing precisely the potential hypoxic tissue harm. Lactate seems to be more related to metabolic acidosis than pH.

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Isoimunization, still a reality!

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Maternal isoimunization occurs in Rh- women when RhD+ fetal cells enter the maternal circulation. The administration of RhD immunoglobulin prevents the formation of anti-D antibody in 99% of cases.

The introduction of Anti-D immunoglobulin reduced the number of cases of D-isoimmunization. A review reported the incidence of Rh sensitization to be 6.8/1000 live births.

The passage of maternal anti-D antibodies to the fetus may lead to anemia, hydrops fetalis, and eventually fetal death.

Case: A 30 year old pregnant women at 16 week gestation was sent to this hospital because of a D-isoimmunization. In her first pregnancy she had been misclassified with an Rh+ blood group and had therefore not undertaken any prophylactic treatment.

At 16 weeks of gestation the first indirect Coombs test placed the titer below critical level (1/16).

The particularity of this case resides in the consistently abnormal rise and fall presented in the antibody titer. Reaching a value of 1/512 at 24th week followed by a value of 1/128 at 26th week gestation.

We monitored the fetal response with repeated measurements of peak blood flow velocity in the middle cerebral artery. There were no signs of fetal hidrops.

At 34th week labor was induced. Although the newborn’s blood group was Rh+, he showed no signs of anemia.

Conclusion: Maternal D-isoimunization may be hazardous for the fetus. In this clinical case the titer reached values greater than critical level with no fetal consequences. Therefore we consider that surveillance may prevent complications.

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Umbilical cord pCO₂ - time to standardize data

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Objective: The gold standard assessment of fetal acid-base status at birth is umbilical cord blood gas analysis. Thus it is of great importance that the results from cord blood gas analyzes are reliable. Our objective was to validate umbilical cord arterial and venous blood gas values, and subsequently describe the values of pCO₂ in relation to specified levels of pH.

Material and Method: Umbilical cord blood gas analyzes were obtained from 7125 term newborns, all participants in the intrapartum multi-center fetal ECG trial (European Union ST Analysis Trial).

Results: From the study group of 7125 the following 1362 cases were excluded; missing cord blood gas values (864), obvious typing errors (7), negative venous-arterial pH difference or negative arterial-venous pCO₂ difference (491). Among the remaining 5763 cases the 5th centile for the venous-arterial pH difference was 0.02 and the 10th centile for arterial-venous pCO₂ difference was 0.06kPa. Cases with lower values were excluded, leaving 5061 validated cases (71% of 7125). We identified centiles for arterial pCO₂ for specified intervals of arterial pH (Table 1).

Conclusions: To our knowledge this is the first study investigating the association between umbilical cord pCO₂ and specified levels of pH in validated data. Blood gas samples should be obtained from both artery and vein to allow for validation. This is essential due to a large number of erroneous samples. Percentiles for arterial pCO₂ for specified arterial pH values can be used to identify cases with high likelihood of breathing before cord clamping.

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Associations between Apgar score and umbilical cord pCO2

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Objective: Apgar score and umbilical cord blood gas values are used for identifying the compromised newborns. The correlation with Apgar score has been explored for pH, but not for pCO2. This study was undertaken to investigate the association between 5 minute Apgar score and cord artery pCO2.

Material and method: Umbilical cord blood gas analyzes were obtained from 7125 term newborns, all participants in an intrapartum multi-center fetal ECG trial (European Union ST Analysis Trial). Samples were validated, excluding cases with missing samples, cases showing an unphysiological or unreliable difference between arterial and venous values. Hence, 5061 cases remained.

Results: A highly significant (p<0.001) difference in umbilical artery pCO2 was found between cases with 5 min Apgar score <7 (n=104) and those ≥7 (n=4957). The median (5th–95th centile range) was 8.3(6.0-12.2) kPa vs. 7.4(5.5-10.0) kPa.

Logistic regression analyzes indicated that 1 kPa gain in pCO2 leads to a 50% increase in odds ratio for 5 min Apgar score <7.

In the <7 Apgar score group 22.1% had pCO2 above the 95th centile (10.1 kPa), compared to 4.5% in the group with Apgar scores ≥7. However, most cases with high pCO2 had Apgar scores ≥7 (Table1).

Conclusions: To our knowledge this is the first published quantification of the association between Apgar score and umbilical cord pCO2. Our Results suggest that a small increase in arterial cord blood pCO2 markedly increases the odds for 5 min Apgar score <7.

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pH less than 7 in umbilical artery cord blood at delivery: labor duration, fetal heart rate tracing patterns and neonatal outcomes

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Objective. To evaluate labor characteristics, cardiotocography (CTG) patterns and outcomes in neonates with cord blood acidosis (arterial pH≤7) at delivery.

Material and Methods. Retrospective study on 4108 women that delivered in our Department from January to December 2007. Arterial cord blood sample was collected from umbilical artery, pH was analyzed. Cases with an arterial pH≤7 were included. CTG was evaluated according to FIGO and Piquard classification during first and second-stage of labor, respectively. Mode of delivery and pregnancy outcomes were reviewed.

Results. We included 24 (0.6%) cases with pH≤7; gestational age was 39+1 weeks (median, 37+3-40+2 weeks IQR). Pregnancies at low risk were 88% of cases. Patients were nulliparous in 71% of cases. Mode of delivery was vaginal in 58% of cases (of which 64% by operative vaginal delivery). Elective caesarean section (CS) and intra-partum CS were performed in 17% and 25% of cases, respectively. Oxytocin was administered during labor in 35% of cases. During first-stage CTG was identified as abnormal or intermediary in 96% of cases. During second-stage, abnormal CTG was observed in 95% of cases, 59% of all cases were characteristic for uterine hyperkinesia. First-stage was shorter compared to Zhang labor curve in 94% of cases, 270 minutes (median, 195-310 minutes IQR). Cerebral palsy was diagnosed in 8% of neonates.

Conclusions. Our data suggest that cord blood acidosis seems to be unrelated to the a priori risk of each pregnancy, appearing to be often a consequence of a short duration of labor.

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Mode of birth and well-being in Germany and USA

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Pregnancy and childbirth may have both positive and negative consequences for women’s health and well-being because of the physical and psychological adaptation. Comparative data on maternal experience with preferred and experienced mode of birth in different countries is rare and does not focus on maternal well-being. Few studies differentiate outcome variables between spontaneous birth, vaginal instrumental delivery, planned caesarean section and unplanned caesarean. This prospective study with data collection in late pregnancy and in the first months after birth compares between German (n=366) and American women (n=39) regarding preferred mode of birth in pregnancy, experienced mode of birth and women’s well-being in pregnancy and post partum. Investigators used a self-administered questionnaire, including validated instruments (WHO-5 Well-Being Index, Sense of Coherence Scale and Edinburgh Postnatal Depression Scale) in both countries. The request for a caesarean section was limited in both samples. Women’s well-being showed an impact on the preferred mode of birth in the German sample but there was no relationship between experienced mode of birth and women’s well-being and postnatal depression scores in both samples. Postpartum well-being for women with elective caesarean section could not be assessed because of the small sample size. Compared to the American mothers German women had lower postnatal depression scores on the EPDS and higher well-being scores on the WHO-5 Well-Being Index. Further cross-national research in this context with higher sample sizes seems necessary.

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Modelling the cascade of interventions

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Aim: We examined the cascade of interventions and the intervals between interventions during labor.

Methods
The ProGeb-Study in Lower Saxony, Germany, included 3963 low-risk women. The sequential relationships between intrapartum interventions – epidural analgesia, amniotomy, oxytocin augmentation – were modeled. The median intervals between onset of labor and the first intervention and between these three interventions were calculated by Kaplan-Meiers estimation. Operative deliveries were treated as censored data. 1322 women receiving none of these interventions were excluded. Significances were assessed by the logrank test.

Results: 1,524 nulliparae (73.9%) and 1117 multiparae (59.6%) received at least one intervention during labor. Of the 268 women who received all three interventions, epidural analgesia was most often the first in the cascade (np: 133, 64.6%; mp: 45, 72.6%). In nulliparae, epidural analgesia (n=580; 27.9%) was the intervention of first choice performed 9.6h after onset of labor. It was followed, 1.5h later, most frequently by oxytocin in 59.1% (n=343) or by amniotomy in 20.5% (n=119, 4.4h). In multiparae, amniotomy (n=629; 33.6%) was most frequently the first intervention, after 4.9h. Following this, multiparae most frequently experienced spontaneous birth (n=503, 80.0%) 0.4h later. The others received oxytocin augmentation (n=99, 15.7%), epidural analgesia (2.4%) or an operative delivery (1.9%).

Discussion: The sequence of interventions differs between nulliparae and multiparae. One-third of the multiparae received amniotomies as the first intervention. Epidural analgesia was the most frequent first choice intervention in nulliparae, very often followed by further interventions.

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Are there any factors predicting amniotomy as the first intervention during labor?

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Aim: We examined factors which predict amniotomy as the first intervention among several administered during labor.

Methods
The ProGeb-Study in Lower-Saxony, Germany, included 3963 low-risk women. Intervals from onset of labor to the first intervention were analyzed by Cox regression, examining amniotomy, oxytocin and epidural analgesia as competing risks. 1322 women were excluded as they had no analyzed intervention during labor. Demographic, fetal, risk-associated and induction-related factors were included as covariates.

Results: In 434 nulliparae and 629 multiparae, amniotomy was the first intervention during the course of labor. The other women received epidural analgesia (n=769) or oxytocin augmentation (n=809) as the first intervention. Membranes were ruptured after median periods of 12.8h after onset of labor in nulliparae and 4.9h in multiparae. 200 (46.1%) nulliparae and 503 (80%) multiparae experienced spontaneous births without any further intervention (50.8%).

In nulliparae, only induction with oxytocin and smaller fetal length were significantly associated with a shorter interval from onset of labor to amniotomy. In third or fourth parae among the multiparae, smoking, lower fetal length, induction with oxytocin or herbal remedies and being without documented risk factors were significant predictors for a shorter interval until amniotomy. Other covariates showed no significant associations.

Discussion: Analysis in multiparae revealed some factors which were associated with an amniotomy as a first intervention during labor, which was rarely followed by any further interventions. In nulliparae, there was a lack of predictors. This study asks about indications for amniotomy and the attitudes of health care professionals when performing amniotomy.

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Length of second stage of labor: influence on mode of delivery and neonatal outcomes

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Introduction: Prolonged second stage of labor is associated with higher operative delivery rates and maternal morbidity, although neonatal outcomes doesn't seem to be modified. Obstetrics parameters like nulliparity, epidural analgesia and Valsalva pushing technique are related with a longer second stage.

Objective: Examine mode of delivery and neonatal well-being and its association with length of second stage of labor.

Methods: Descriptive correlational design. Sample of 156 women with singleton gestation, cephalic presentation, epidural analgesia, delayed pushing and live births at a University Hospital in Comunidad de Madrid.

Measured Variables: Length of second stage of labor in minutes.

Mode of delivery: spontaneous vaginal delivery or not spontaneous vaginal delivery (instrumental and caesarean section). Umbilical artery pH. Apgar score. Other variables (maternal age, pre-pregnancy weight, weight gain until labor, labor induction, neonatal weight, gestational age, previous vaginal deliveries) were analized as potential confounders.

Results: Mode of delivery: the duration of second stage (OR=1.468; 95% IC=1.071 to 2.012) and previous vaginal deliveries (OR=0.183; 95% IC=0.048 to 0.700) were factors that influence the mode of delivery.

Neonatal outcomes: negative correlation between duration of second stage and umbilical artery pH was found (p=-0.212; p=0.009).

Conclusions: A greater length on second stage of labor needs an intensive surveillance, to assure a safe and effective management of this period. Obstetric caregivers should evaluate and anticipate adverse effects of prolonged second stage.

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Effects of spontaneous and instrumental vaginal delivery on perinatal outcomes

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Objective: To compare the perinatal outcomes on spontaneous and instrumental vaginal deliveries.

Material and Methods: From January 2003 to December 2008 a retrospective research, with 21,678 vaginal deliveries, was done in Virgen de las Nieves University Hospital. Two groups were obtained according to the way of the ending of the vaginal delivery: In the group I (n: 17,196) the spontaneous vaginal deliveries were included and the group II (n: 4,482) was performed by the instrumental vaginal deliveries. We used the next obstetric instruments: the spatulas (n: 1,736), the vacuums (n: 1,539) and the forceps (n: 1,553).

Results: The average gestational age was 274±36 days in the group I and 276±15 in the group II. The weight of the newborns was 3,181±530 grams (g) and 3,246±494g. respectively. In the group I the apgar scoring was 8.67±1.5 on the first minute and 8.97±0.9 on the five minutes; in the group II it was 8.3±1.2 and 8.87±0.6. The arterial pH was 7.26±0.12 in the spontaneous deliveries and 7.21±0.45 in the instrumental group. The vein pH was 7.31±0.21 and 7.25±0.11 in each one. When all these variables were compared, there were statistical differences in every field (p<0.001).

Conclusion: The group of deliveries that finish in an instrumental vaginal way is defined by a worst perinatal outcome, that can be explained because the pregnant women´s population is different, with a greater gestational age and weight of the newborns.

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A comparison between different episiotomy types during vaginal delivery

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Objective: to study different episiotomy types and the benefits of an episiotomy during the second stage of labor.

Materials & Methods: Participants: 1696 women who vaginally delivered a live full term, singleton baby between 2003 and 2008 in our department (obstetrics & Gynecology clinic of General hospital of Pyrgos, Greece). Age between 14 and 44. Of the total of 1696 women included in the study 66 were primiparous the rest were multiparous. 1485 women received an episiotomy, 211 did not received an episiotomy but experience a second, third or fourth degree spontaneous perineal laceration. The types of episiotomy performed on women were midline episiotomy, mediolateral, hockey stick episiotomy (modified median episiotomy) and rare horizontolateral. The statistic analysis of the Results was done with method SPSS (prices of p<0.05 were considered as statistically important).

Results: Midline and hockey stick episiotomy heals easier than mediolateral and horizontolateral episiotomy. Dyspareunia was significantly higher in the mediolateral and horizontolateral episiotomy. Midline episiotomy increase the incidence of third-and-fourth-degree lacerations. Rectovaginal fistulae was significantly more common after a midline procedure. Hockey stick and median episiotomy were associated with lower rates of significant hematoma than mediolateral and horizontolateral episiotomy.

Conclusion: In cases where an episiotomy is indicated a hockey stick episiotomy (modified median episiotomy) is preferable to a median incision.

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Perinatal outcome in a second pregnancy depending on a previous caesarean or vaginal delivery

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Introduction: The aim is to evaluate whether perinatal outcome in a second pregnancy depends on previous way of delivery.

Methods: A cohort of 3155 women with just one previous child was selected from a total 10713 singleton births (29.45%). We compared 623 (19.7%) patients with a previous caesarean section with 2532 (80.3%) vaginal delivery. We contrast perinatal outcome, type of birth, labor induction and puerperal complications. Potential confounding variables were adjusted by logistic regression.

Results: The group with previous caesarean showed higher mean age (32.21 vs. 31.57 years, p<0.05), more frequently labor inductions (19.1% vs. 12.7%; p<0.05), and a greater proportion of both instrumental deliveries (21.5% vs. 3.8%; p<0.05) and caesarean sections (50.9% vs. 9%; p<0.05). A previous C-section was also associated with a greater number of fetuses with birth-weight ≤P10 (10.1% vs. 7.4%; p<0.05). Puerperal complications, both mild (4.3% vs. 2.6%; p<0.05) and severe (6.1% vs. 1.8%; p<0.05), were increased in the previous C-section group. No differences were found for sex, gestational age at birth and scores below 7 in the Apgar 5 minutes test. The adjusted odds ratio for the group with previous caesarean section was 10.91 (CI 95% 8.81-13.51; p<0.005) for the conduct of a caesarean section, 1.41 (CI 95% 1.04-1.91; p<0.005) to have a birth weight ≤P10, and 3.37 (CI 95% 2.16-3.25; p<0.005) for the development of serious complications in the puerperium.

Conclusions: A previous caesarean section is associated with an increased risk of worse perinatal outcome and puerperal complications in second pregnancies.

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Cervical dilatation at the time of caesarean section may affect the success of a subsequent vaginal delivery

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Objective: To evaluate the effect of labor progress prior to caesarean delivery on the outcome of vaginal birth after caesarean delivery (VBAC).

Methods: The medical records of women attempting VBAC between January 2000 and February 2008 were reviewed. All women had only one previous caesarean and underwent spontaneous labor.

Results: Among 1,148 enrolled women, 956 (83.3%) achieved a successful VBAC. Birth weight, previous indication for caesarean delivery, and oxytocin augmentation were significantly associated with VBAC outcome. By multivariate analysis, a cervical dilatation ≥ 8cm at previous caesarean was independently predictive of successful VBAC in women with a previous caesarean for non-recurrent indications (p=0.046), yielding a VBAC success rate of 93.1%, whereas the extent of cervical dilatation at the previous caesarean did not affect the outcome of subsequent delivery in women with a previous caesarean for recurrent indications.

Conclusions: Women with caesarean for non-recurrent indications who achieved a cervical dilatation ≥ 8cm may be the best candidates for VBAC, with the greatest likelihood of a successful VBAC. Labor progress at previous caesarean can serve as a valuable indicator for VBAC outcome in women with a previous caesarean for non-recurrent indications, and therefore should be discussed as part of preconception counseling.

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Caesarean section by vertical incision of lower uterine segment

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Objectives: to analyze the use of vertical incision in lower uterine segment (LUS) when performing Caesarean section (CS). Methods. 89 pregnant women who delivered by CS are included: main group (40) with vertical incision in LUS (preliminary intention, but final decision during surgery) and controls (49) with transverse incision of LUS with difficulties/complications in fetus extraction (20 with uterine lacerations and 19 with T-form incision). Mean gestational age in main group is 32 (range 26-39) vs. 31 in controls (27-39). Results. Longitudinal incision is performed in 57.5% for prematurity and no space for transverse incision (LUS not formed), in 25% for situs transversus of fetus; the rest are related to difficulties in isthmicotransverse approach (myoma praevia, anomalies, adhesions of omentum). Duration of CS is mean 66 min. in main group vs. 74 min. with controls (p<0.05). Time to extraction of fetus is less than a minute in main group vs. more than a minute with controls. No lacerations are found with vertical incision of uterus. Blood loss in main group is 664ml, vs. 884ml in controls (p<0.05). Mean pH from umbilical artery of newborns is 7.259 in main group vs. 7.19 in controls (p<0.05); Apgar at 5-th min. is 7 vs. 6.

Conclusions: Vertical incision of LUS before the latter is formed with situs transversus of fetus and difficult approach ensures less lacerations, less birth trauma with better final neonatal outcome.

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Multiple repeat caesarean section and hysterectomy cesarea

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Hysterectomy cesarea is a type of hysterectomy done immediately after the caesarean section. The aim of the paper: To determine whether a greater number of Caesarean sections statistically increases the number of hysterectomy cesarea and postpartal hysterectomy, especially after the third caesarean section.

Materials and methods used: retrospective study from January 1st 1987 to December 31st 1998. which included 2474 repeat caesarean sections. There were 2041 women with two caesarean sections, 343 women with three caesarean sections, 74 women with four caesarean sections and 16 women with five caesarean sections. A comparative study was made on the frequency of hysterectomy cesarea and postpartal hysterectomy after the first and the second and after the third and the fourth caesarean section as well as after the three previous caesarean sections compared with the group of women after the fourth caesarean section.

Results: The frequency of hysterectomy cesarea in the group of women after the second caesarean section was 0.44% and after the third 1.46%. After the fourth caesarean section a hysterectomy was done 1.35% and after the fifth caesarean section there were no cases of hysterectomy cesarea. The differences are not statistically significant. Postpartal hysterectomy after the second caesarean section was done 0.93%, after the third 0.87%. The differences are not statistically significant. After the fourth and the fifth caesarean section there were no cases of postpartal hysterectomy.

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Characteristics of the lower uterine segment with multiple caesarean section

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The aim of the paper: To determine whether a greater number of caesarean sections statistically makes a difference in pathohistological quality of the scar especially after three previous caesarean sections in comparison with the fourth one.

Materials and methods used: prospective study conducted on Clinics of Gynecology in Pristina from January 1st 1997 to December 31st 1998. There had been 374 repeat caesarean sections. The scars were compared after the first and second and after the third and fourth caesarean section as well as after the previous three in comparison with the scar after the fourth caesarean section.

With all iterative caesarean sections the specimen was taken from the surgery cut distal edge. The specimens were fixed in 10% formalin and the preparations were colored with Hematoxylin – eosin using Van Gieson’s method. A degree of mononuclear reaction in miometrium was determined, a degree of desmoplasia and the quantity of blood vessels.

Results: the Results of our research show that we did not find a statistically significant difference in the mononuclear reaction degree, the degree of desmoplasia and the quantity of blood vessels in the scar compared after the first and second and after the third and fourth caesarean section as well as after the previous three in comparison with the scar after the fourth caesarean section.

Conclusion: With the increased number of caesarean sections there is not a statistically significant difference in the pathohistological quality of the scar.

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Full-term delivery after embolization of uterine artery with N-Butyl Cyanoacrylate for abruptio placentae: A case report

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Introduction: Perinatal hemorrhage is a major cause of maternal death. There are some reports that transcatheter arterial embolization: TAE is effective in managing perinatal hemorrhage and is able to avoid hysterectomy. We report a case of a patient who became pregnant naturally and underwent elective caesarean section after embolization of uterine artery with permanent embolic agents: N-Butyl Cyanoacrylate (NBCA) for abruptio placentae

Case report: A 35-year-old gravida 2 para 0 at 32 week of gestation presented for emergency caesarean section because of abruptio placentae. The new born died at day 0. Blood loss during the operation was 4750ml. After the caesarean section, we found hematoma about 4cm in diameter at the uterine incision. As the size of the hematoma was increased continuously, pelvic angiography was performed 13 hours after the caesarean section. extravasation was observed from both right and left uterine arteries. At first, uterine embolization was performed by gelatin sponge (Gelform), but extravasation did not disappear. Next, we used NBCA (histoacryl) for embolization. Then, extravasation stopped rapidly. Total transfusion was 10,190ml. Nine months after the caesarean section, she became pregnant naturally. At 37 week’s gestation, she delivered a boy (3,132g) by elective caesarean section with Apgar score 9/10. CT angiography performed postpartum showed arteries at the position of uterine arteries bilaterally.

Conclusion: NBCA was effective for perinatal hemorrhage the primary case of maternal death, to avoiding hysterectomy. Here, we report a case in which fertility was presented after the procedure.

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Management of a placenta previa percreta with fundal incision and caesarean hysterectomy

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Abnormal implantation of the placenta into the uterine wall Results in placenta accreta and percreta, affecting approximately 1% of all pregnancies. Known risk factors are previous uterine surgery such as curettage and caesarean deliveries. Complications include damage to adjacent organs and hemorrhage leading to hysterectomy. In the reported case a 43-year-old woman, gravida 10 para 4, was referred to our center at 19 weeks’ gestation with vaginal bleeding and major placenta previa. Her medical history showed six curettages after pregnancy loss, one vaginal birth and two caesarean sections due to placenta previa. On the sonographic examination there was an obvious loss of the retroplacental hypoechoic zone as well as presence of placental lacunae and hypervascularity of the interface between uterine serosa and the posterior bladder wall. These findings were confirmed on MRI. After PPROM at 32+2 weeks’ gestation a female newborn (1,490g, 41cm, APGAR 7/8/9) was delivered by caesarean section with fundal incision. Afterwards hysterectomy with partial resection of the posterior bladder wall was performed. Prior surgery bilateral uretral double-J catheters had been placed. The overall blood loss was 15,000ml requiring mass transfusion. After two days in ICU for further monitoring she was transferred to the obstetrical department and released on the 15th postoperative day. The neonate was discharged from NICU on the 22nd day of life. This case stresses that placental implantation disorders can be life threatening even if the diagnosis is known and peripartal management with interdisciplinary intervention is planned in a tertiary care center.

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Transverse fundal uterine incision for placenta previa

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Cesarean section (C/S) for placenta previa (PP) carries a high risk of severe blood loss. Additionally, approximately half of patients with PP and two previous C/Ss have placenta accreta/increta/percreta. We performed the transverse fundal uterine incision (TFUI), originally described by Shukunami et al. (J Matern Fetal Neonatal Med 16:355, 2004), in two cases of PP on the previous caesarean scar.

Case 1: At 36 weeks, an elective C/S was performed in a 33 y/o woman, gravida 3, para 2 (C/S twice) with PP covering the previous caesarean scar. A healthy male neonate (2,850g) was delivered via a TFUI. The placenta was removed manually while a rubber tube placed around the cervix served as a temporal tourniquet to reduce blood flow. The total blood loss was 1,353ml.

Case 2: At 35 weeks, an elective C/S was performed in a 34 y/o woman, gravida 6, para 3 (three C/Ss) with PP suspected to accompany placenta increta or percreta. A healthy female baby (2,765g) was delivered via a TFUI. Preoperative preparations included ureteral stent placement and insertion of catheters into pelvic arteries. Attempts to preserve the uterus were abandoned when placenta percreta was diagnosed by visual inspection. The patient underwent hysterectomy after uterine artery embolization. The total blood loss was 1374ml. Heterologous blood transfusion was avoided in both cases.

Conclusions: The TFUI can avoid catastrophic hemorrhage associated with an incision through PP, and may serve as a key component of multidisciplinary management for PP complicated with accreta/increta/percreta.

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Antenatal versus postnatal management of placenta accreta/percreta in a French tertiary care centre: 27 cases over a two years experience

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Objective: This study was designed to evaluate our results in the management of placenta accreta or percreta, and to compare the impact of an antenatal transfer versus a postnatal transfer to our multidisciplinary care unit.

Methods: We ran a retrospective observational study including all the patients treated in our unit for placenta accreta or percreta between January 2007 and December 2008. Indoor patients and cases of antenatal transfers (Group A) were compared with postnatal transfers (Group B).

Results: Twenty seven patients presenting with a placenta accreta or percreta were included. Seven patients were initially followed up in our hospital for their pregnancy and 4 patients were transferred during the antenatal period (Group A); 16 during the postnatal period (Group B). Ten patients out of eleven (90.9%) in group A benefited an antenatal diagnosis and conservation of the placenta at delivery. For Group B, 3 cases of abnormal placentation were antenatally diagnosed (18.75%) and 13 cases were diagnosed at delivery (81.25%). The comparison of Group A versus Group B showed fewer rates of hemorrhagic shocks (9% vs. 50%), transfusion (18% vs. 50%), with fewer transfusion volumes, disseminated intravascular coagulation (9% vs. 50%), UAE (9% vs. 43.7%) and emergency surgical procedures (0 vs. 25%) for Group A.

Conclusion: Placental conservation with or without uterine conservation greatly improves the maternal morbidity in cases of abnormal placentation. The prognosis is significantly improved when patients are treated in specialized care units since the antenatal period.
Conservative management of partial placenta accreta/increta

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Introduction: Due to the increasing number of caesarean sections, placentation disorders in consecutive pregnancies are increasing. The management of placenta accreta/increta, as a condition of the entire placenta, is increasingly discussed. Nevertheless there is only little information regarding the management of partial or focal placenta accreta/increta, and the risk of severe complications such as bleeding and infection may be underestimated.

Patients and Methods: We report about 5 cases of focal placenta accreta/increta where conservative management was attempted. 2 patients were treated postpartum with methotrexate (MTX) and folinic acid, 2 patients did not receive chemotherapy, but received regular follow up examinations, one patient underwent an hysterectomy.

Results: In 1 patient a hysterectomy had to be performed due to severe hematometra, atony and severe bleeding.

In the other 4 patients fertility could be preserved. One case with MTX + folinic acid was complicated by endomyometritis, another case without chemotherapy by severe hematometra. All 4 patients eventually underwent therapeutic curettages. Three D&Cs were performed without further complications, one patient suffered from major bleeding.

Discussion: Four out of 5 patients with partial placenta increta could be treated conservatively. MTX and folinic acid showed no benefit in our small case series. Regarding breast feeding, the necessity of chemotherapy might need to be reconsidered.

Patients with conservatively managed partial placenta accreta/increta must be followed up closely. Digital vaginal examinations should be avoided and speculum examination under strict sterile conditions instead performed. Curettage is advisable, once the demarcation of the focal placenta residuals can be visualized sonographically.

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Objective: To analyze blood loss with or without UAE in caesarean section of placenta accreta.

Methods: Among 206 pregnant women with placenta previa were delivered in the National defense medical college hospital from 1989 to 2008, 15 were pathologically diagnosed placenta accreta. Before May 2004, five cases were performed a caesarean hysterectomy (non-UAE group). One case was excluded from the analysis because the placenta was not removed, methotrexate was administrated during the operation and hysterectomy was performed. After May 2004, 8 cases were not removed placentas and performed a UAE subsequent to caesarean section of placenta accreta (UAE group) except for one case was not able to diagnose before caesarean section. Historical observation studies for an amount of blood loss and transfusion were performed.

Results: A comparison of the amount of blood loss of caesarean section, the total of blood loss of non-UAE group and UAE group were 6,609±2,773ml and 2,708±2,337ml, respectively (p=0.040). An amount of packed red blood cell transfusion of non-UAE group and UAE group were 4-58 units and 4-12 units (p=0.033) and an amount of fresh frozen plasma transfusion of non-UAE group and UAE group were 0-40 units and 0-16 units, respectively (p=0.033).

Among UAE group, 4 cases (4/8, 50%) could be managed without hysterectomy because a placenta was delivered transvaginally.

Conclusion: It is possible to decrease an amount of blood loss and transfusion of caesaren section of placenta accreta with UAE. Additionally, this Result suggests the possibility of uterine sparing in placenta accreta.

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Is it reasonable to delivery all apparently uncomplicated monochorionic twins by c-section?

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Background: Several authors advocate c-section delivery in all otherwise uncomplicated monochorionic diamniotic twin pregnancies due to the residual risk of fetal death intrapartum.

Material/Methods: A database of 576 completed multiple pregnancies during 1996-2007 was reviewed. The uncomplicated 111 monochorionic diamniotic (MCDA) twin pregnancies delivered after 24 weeks were selected (exclusions: twin-twin transfusion syndrome, growth restriction, discordant growth, structural abnormalities, monoamnionicity, twin reversed arterial perfusion sequence, high-order multiple pregnancies). We evaluated type of delivery, gestational age (GA) at delivery, and morbimortality of newborns. The Results from MCDA were compared to those of the 291 uncomplicated dichorionic diamniotic (DCDA) twin pregnancies in the same period.

Results: Three unexpected single intrauterine deaths occurred in three (2.7%) of 111 previously uncomplicated MCDA pregnancies, at a median GA of 33±2 weeks. Two of the deaths occurred during delivery at 33 (first twin in a c-section delivery for fetal distress in a non-stress testing) and at 35 week (presenting twin in a vaginal delivery). GA at delivery was 34.5±2.6 weeks and vaginal delivery occurred in 60.4% of these pregnancies. Eleven unexpected single intrauterine deaths occurred in nine (3.1%) of the 291 previously uncomplicated DCDA pregnancies. GA at delivery was 34.8±2.9 weeks and in these pregnancies delivery occurred by c-section in 51.4%. There were no statistical significance in the unexpected single intrauterine deaths occurred in MCDA twins when compared to DCDA (p=0.57) as well as on GA at delivery and newborn weights.

Conclusion: In otherwise apparently uncomplicated MCDA pregnancies is not reasonable to delivery all by c-section.

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Investigation on perinatal prognosis of twins

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Objective: Infertility treatment has been pointed out to promote the increase of multiple gestation. We investigated the perinatal prognosis in twins in our medical center and discussed the perinatal management in twins.

Methods: Study was performed on 926 twins between January 1996 and December 2008. We compared the maternal age, number of gravida, infertility treatment, day of delivery, delivery maneuver, bleeding, weight, APGAR score, umbilical pH and discordancy. In cases with the first twin to be nonvertex, elective caesarean delivery was undergone, while in other cases the delivery maneuver was decided depending on obstetrical factors. Study was performed using Kruskal-Wallis Test for mean value, Pearson’s chi-square Test for Cross tabulation and the Results were considered statistically significant for p values <0.05.

Results: Of 928 twin deliveries including 2 Monoamniotic Monochorionic twins (MM), 361 were Monoamniotic Dichorionic twins (MD) and 565 were Diamniotic Dichorionic twins (DD). Maternal age, the birth weight and APGAR score were lower in MD than in DD (p<0.01). There was no discrepancy in delivery maneuvers between MD and DD. Both MD and DD showed similar number of vaginal birth and caesarean section cases. Cesarean section of the second twin after vaginal delivery of the first twin was performed in 11 cases of MD and in 16 of DD.

Conclusion: This research shows that vaginal delivery can be safely performed in twins under the circumstances that caesarean delivery can be swiftly arranged if any difficulties arise.

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Perinatal and obstetric parameters in naturally conceived (NC) triplet pregnancies versus assisted reproductive therapy (IVF/ICSI) 1/2000-3/2009

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Evaluation of 12 triplet pregnancies: 4 NC; 3 IVF, 6 ICSI. Mean maternal age in the IVF/ICSI-group was 34, 29 for the NC-group. Parity: NC: 2xIP, 1xIIP, 1xIVP; ICSI: 4xIP, 2xIIP, IVF: 2xIP, 1xIIP. Chorionocity: NC 100% tri/tri; ICSI: 5xtri/tri, 1xbi/tri; IVF: 1xtri/tri, 2xbi/tri. Weight in IVF for the first and second child was on average 300g lighter than for ICSI and NC children.

4 NC triplets tri/tri. No feticide, no IUFD. One patient demonstrated GDM and PE.
2 feticides after ICSI/IVF, 3 IUFD, 1 embryo loss. No pH<7.19 with NC and IVF/ICSI. No birth defects. Two of five ICSI patients recorded a feticide, tri/tri. Two female IUFD with bi/tri in the 33rd week of gestation. C-section rate for all triplets born as three was 100%; one vaginal birth as twins in the ICSI-group, after feticide. Weight of all children after NC and ICSI: around 1900g. Mean gestational week at delivery: 34 (NC, ICSI/IVF).

IVF/ICSI-group demonstrated a higher rate of severe perinatal complications, which is also cause by chorionocity (bi/tri). Lower maternal age in NC-group. There were differences in the IVF/ICSI group with regard to IUFD/feticide. No remarkable aspects in parity. In-patient hospital duration for NC and IVF/ICSI is high. No remarkable aspects were seen with regard to mode of delivery, fetal birth weight, sex of the children, nor week of gestation. No live-born child had a pH<7.19. However, prominent were the perinatal complications in the IVF/ICSI-group.

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Mode of delivery in patients from Macedonia with multiple pregnancies formerly and now

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Background: Over the past 20 years, the number and rate of multiple births have dramatically increased in Macedonia. The rise in multiple births is mainly attributable to the increased use of ovulation-inducing drugs and the newly developed assisted reproductive technologies such as in vitro fertilization. In this article, the management of the labor and delivery of multiple gestations are reviewed.

Material and Methods: Multiple pregnancies were analyzed in 2007 and 1997. The patients were divided according to the mode of delivery. The research was made on the patients that were delivered in University Clinic for Gynecology and Obstetrics in Skopje, Macedonia.

Results: In 1997 there were 55 multiple pregnancies (1.15% from all delivered patients). 16 from them were delivered by Caesarean Section and 39 spontaneously (29.1% and 70.9% respectively). In 2007 there were 103 multiple pregnancies (2.54% from all delivered patients). 68 were delivered by Caesarean Section and 35 spontaneously (66% and 34% respectively).

Conclusions: Because multiple gestations are associated with an increased risk of perinatal morbidity and mortality and an increasing percentage of low-birth-weight infants, preterm births, and infant mortality, nowadays, Caesarean Section is more commonly used as the preferred mode of delivery in our country.

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Maternal and neonatal outcome of twins delivery depending on mode of delivery

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Introduction: The increasing incidence of twin pregnancies together with the caesarean delivery, has resulted in intense scrutiny of the most appropriate method of twin delivery. The aim of this study was to compare maternal and neonatal outcome of twin births according to mode of delivery.

Methods: Retrospective analysis of medical records of 276 women with twin pregnancy who had deliveries of both twins at our department between January 2001 and December 2008 was performed.

Results: The Results will be presented later based on maternal age, parity, gestacional age, maternal antepartum and postpartum complications, fetal presentations, birth-weight, mode of delivery of each twin and Apgar scores.

Conclusions: The mode of twin delivery, whether vaginal or by caesarean section, would depend on the judgment and expertise of the labor in twin gestations.

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Breech presentation-mode of delivery and early neonatal outcome

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Objective: To compare early neonatal outcome in vaginal delivery vs. planned or urgent caesarean section for breech presentation delivered after 28 weeks and weighing more than 1000g.

Materials and Methods: A retrospective study of 505 single live born breech neonates delivered in our Institute from 1.1.2007.-31.12.2008. We analyzed Apgar-5, early neonatal morbidity and mortality, duration of stay in the Neonatal intensive care unit/NICU/according to birth weight and gestational age. Statistical analysis: Chi-squared likelihood ratio, Mann-Whitney and Student's t-test.

Results: Delivery modes: vaginal delivery/VD/-205/40.6%/, planned caesarean section/CS/-157/52.3%/and urgent CS-143/37.7%. Apgar-5 scores were significantly higher after planned CS compared to VD/p=0.023; p<0.05/and urgent CS/p=0.016; p<0.05/. There was no difference between VD and urgent CS/p=0.022; p>0.05/. Apgar-5 was not affected by mode of delivery for neonates with birth weight<1500g. Asphyxia, respiratory distress syndrome and intraventricular hemorrhagia complicated 17.1% vaginal deliveries,16.8% planned CS and 31.8% urgent CS. According to birth weight early neonatal outcome was better after planned CS comparing to VD/p=0.015; p<0.05/and urgent CS/p=0.012; p<0.05/as well as after VD comparing to urgent CS/p=0.012; p<0.05/. Gestational age at delivery had the strongest influence on neonatal morbidity after vaginal delivery/p=60.32; p<0.05/. The longest stay in NICU was after vaginal delivery at 34-36 weeks/28+/-26 days/ and after urgent CS performed before 33 weeks/43+/-25 days/. Early neonatal deaths were 7 per 1000 births, three occurred in vaginal delivery group.

Conclusion: Planned caesarean section is recommended as the mode of delivery for fetuses in breech presentation with estimated birth weight more than 1,500g and at gestation age more than 33 weeks. We could not conclusively resolve if caesarean delivery was advantageous for neonates of less than 33 weeks whose birth weight was lee than 1500g.

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Breech deliveries in the maternity hospital in Sremska Mitrovica in the period from 2000-2008

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Introduction: Obstetricians are still put into a dilemma when they have to deal with breech presentation of a fetus, when they must decide how to complete a delivery, and which technique to choose. This dilemma is still an subject of many discussions amongst experts. The approximate average number of childbirths in hospital is 1400 per annum.

The aim of the work: We have observed the number of breech deliveries during the period from 2000-2008. Especially concerning with ways of completing the deliveries and average. Apgar score which each child was given depending on the way of finishing the delivery.

Results: The total number of deliveries is 12859.

The total number of Presentatio pelvina is 477 (3.7%) for the period. Total number of Sectio cesarea is 2707 (21%).

From 477 breech deliveries 339(71%) was finished by Sectio cesarea and 138 (29%) by manual help. Apgar score in Sectio cesarea was 8. and in manual help was 7.

Discussion and conclusion: The total number of breech presentation in our region fit with data from literature (3-5%). It is obvious that the number of deliveries finished by using Sectio cesarea dominates, although there is no tendency to increase the number. The breech presentation is still not an absolute indication for using Sectio cesarea in our hospital. The Apgar score which stays relatively equal justifies our scope of indication for finishing pregnancies, although the leading of breech deliveries and making decisions on the ways of finishing pregnancies are to be left to the most experienced obstetricians and to the working team-obstetrician, neonatologist.

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**Term breech and early neonatal outcome-caesarean sections vs. vaginal breech delivery**

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Objective: To evaluate early neonatal outcome of term breech fetuses after vaginal delivery and planned or urgent caesarean section.

Materials and methods: A retrospective study from 401 singleton live neonates delivered vaginally or by caesarean section at a gestational age greater than 36 weeks in our Institute during 2-year period /1.1.2007-31.12.2008/. We analyzed birth weight, Apgar score at 5th min., early neonatal morbidity and mortality and duration of stay in the Neonatal intensive care unit/days/. Statistical analysis: methods of descriptive statistics and Student's t-test.

Results: The following groups with respect to the mode of delivery were included: vaginal breech delivery in 139/34.6%/; planned caesarean section/CS/ in 134/33.4%/ and urgent CS in 128/31.9%/.

Lowset maneuver was performed in 88.5% cases. Mean birth weight was 3,200+/−625g in vaginal and 3,350+/−543g in caesarean delivery /p<0.05/. We did not find difference in Apgar-5>8 among three groups /96.4%,94.5% and 97.7%, respectively; p>0.05/. Frequency of asphyxia, respiratory distress syndrome and intraventricular hemorrhagia was significantly higher after urgent CS comparing to vaginal delivery/24.2% vs.9.6%, t=3.74; p<0.01/ and planned CS /24.2% vs. 12.6%, t=2.45; p<0.05/. There were no difference in early neonatal complications between vaginal delivery and planned caesarean section/t=0.86; p>0.05/. Neonates stayed significantly longer in the Neonatal intensive care unit after urgent caesarean section comparing to vaginal delivery/7.21+/−10.74 days vs. 5.23 +/−2.89 days, p=0.000; p<0.05/ and planned caesarean section /7.21 +/−10.74 days vs. 5.34 +/-2.88 days, p=0.037; p<0.05/. No early neonatal deaths occured during study period.

Conclusion: Our Results support that a trial of labor may be offered to patients with breech presentation at term. We advocate that performing vaginal breech delivery should be restricted to experienced personal.

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Reverse breech extraction in cases of impacted fetal head during second stage cesarean section

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Introduction: Second stage Cesarean Section (CS) is associated with a higher risk of maternal morbidity especially in cases with fetal head impaction. The standard recommended procedure in these cases is to gently disengage the fetal head from the pelvis employing in some women a vaginal pressure to push up the impacted fetal head.

Objective: To explore whether a reverse breech extraction maneuver at second stage CS is feasible and to examine fetal and maternal morbidities employing this maneuver.

Setting: A community hospital.

Design: A prospective cohort study during a period of 3 years.

Patients: Women with urgent CS performed at second stage with full dilatation and fetal head impaction were recruited to this study.

Outcome measures: Estimation of blood loss, blood transfusion, drop of hemoglobin, need for J or inverted T shape incision, inadvertent extension of incision as well as postpartum hemorrhage, fever, scar infection and urinary tract infection. In addition, Apgar score at 1'/ 5', umbilical cord PH, fetal trauma and admission to neonatal ICU.

Results: The total number of deliveries during the period of the study was 5710. Of which 1206 (21%) were performed by CS including 815 (14%) by emergency CS. Twenty five cases were performed at full cervical dilatation with an impacted fetal head employing the reverse breech maneuver. The mean age of women was 26.9+3.2 years, all at term between 38+5 and 41+6 weeks of gestation. The mean gravidity and parity was 2.1+1.7 and 1.1+1.7, respectively. The mean fetal weight was 3,540+474gm. and the mean time of full cervical dilatation was 106+53 minutes. All CS were performed in low transverse-incision. In two cases the incision had to be transformed to a J or inverted T shape. None of the cases had an inadvertent extension of the uterine incision. The mean estimated blood loss at CS was 580+100ml and the mean hemoglobin drop following operation was 1.8+0.7gm%. None of the women in the study needed a blood transfusion. The Apgar scores of newborns at 1' and 5' were 7.9+1.6 and 9.4+0.6, respectively. Umbilical cord PH was 7.27+0.05 and none had a PH lower than 7.15. As well, none of the newborns had a trauma related to the reverse breech extraction or were admitted to the neonatal ICU. All women following CS had uneventful postpartum period with no complications.

Conclusion: Our study shows that the reverse breech extraction is feasible in cases of second stage emergency CS with an impacted fetal head. Maternal as well as fetal complications following this maneuver seem to be low.

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**External cephalic version. A new procedure in our hospital**

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Considerable disagreement surrounds the management of breech presentation, particularly with respect to the place of external cephalic version (ECV). Reported series of cases have reported very low complications rates with ECV (Impey 2005). Attempting ECV reduces the chance of non-cephalic birth and caesarean section (Cochrane Database Syst Rev. 2006).

We were implementing ECV in our service one and a half years ago. Now we routinely offer ECV to all patients with transversal or breech presentation near term (35-37 weeks), if there is no contraindication. (n=74).

We have an immediate success rate of 50%. In the successful group the percentage of vaginal deliveries was 83%(30/37). This represents a 41% of the total (30/74). In the successful group we had done seven caesarean sections. The most common cause was spontaneous reversion to breech position (57%, 4/7), a case of placenta abruptio 4 weeks post-release and two cases of suspected fetal distress.

In the unsuccessful group the caesarean section rate was 97%. There is a vaginal delivery in this group, in a case of a spontaneous version.

There have been six cases with complications (8, 1%): transient abnormal baby’s heart rate (2, 7%), vaginal bleeding and emergency caesarean section (1, 3%), and transient bradycardia (2, 7%).

**Conclusions:**
- ECV is an effective procedure for increasing the chance of cephalic presentation.
- ECV is effective in decreasing the rate of caesarean delivery.
- ECV has a small procedure-related risk, and is a safe procedure.

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First experiences with the Cook-catheter: How efficacious is cervical ripening with the double-balloon device?

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Introduction: The incidence of labor induction in developed countries is rising. High risk patients who have had a previous Caesarean section need safe induction methods to avoid uterine tachysystole and rupture. Mechanical methods for cervical ripening play a secondary part in modern obstetrics. We present our first results with the Cook-catheter, a double-balloon device.

Methods: Twenty nulli- and primiparous patients with an unfavorable cervix at 38-42 weeks gestational age and one multipara took part in our study. Entry criteria included a singleton pregnancy, cephalic presentation, intact membranes and normal position of the placenta. A 50ml balloon was placed just beyond the internal os during a sterile speculum examination, and the second 45ml balloon was inserted in the vagina near the external os. The Cook-catheter was removed after a predefined time of twelve hours.

Results: The catheter could be inserted without difficulty. Prostaglandin E2 administration was required after catheter removal for labor to begin. Only in the case of the multipara did rupture of membranes and labor occur a few hours after catheter insertion. One Caesarean section was carried out due to failure to progress, while the other patients achieved a vaginal delivery with normal neonatal outcome.

Discussion: Little experience with double-balloon device exists. The use of the Cook-catheter seems to be promising. Before any final conclusions about safety and efficacy of this induction technique can be made, especially in women with previous Caesarean section, randomized controlled trials are warranted.

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Lactate concentration in amniotic fluid during labor, a good predictor of labor dystocia

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Maternal and fetal morbidity is associated with prolonged labor. Inefficient uterine activity might lead to anaerobic metabolism in the myometrium with extended lactate production. Elevated lactate concentration in myometrial tissue might be reflected by high lactate concentration in amniotic fluid (AF). Previous work showed a good correlation between high lactate level in AF and operative intervention due to dystocia.

Objective: To study if high lactate concentration in AF in dysfunctional labor could be used as a better predictor of labor outcome than the partogram alone. Dystocia was defined as whether action line was passed or when no progress of labor was made within 2 hours.

Study design: Observational. AF from 825 women was collected during labor. Inclusions criteria for the study were: normal pregnancy, >37 weeks, regular painful contractions, ruptured membranes and a cervical dilation ≥3cm. A partogram was recorded for every women participating in the study. Lactate concentration, way of delivery, and maternal/fetal complications were recorded.

Results: 24% of the 825 women had an operative intervention due to dystocia. If the lactate concentration in AF was >12.0 mmol/l when labor was arrested/slowly progressing, 78% of the women were operative delivered due to dystocia. If lactate level was <10.2 mmol/l, 76% had a spontaneous normal delivery.

Conclusions: Lactate concentration in AF can be used as a good predictor of labor outcome. High lactate concentration has a good correlation to instrumental delivery; low lactate concentration has a good correlation to spontaneous vaginal delivery.

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Induction of labor with misoprostol – obstetric and perinatal outcomes

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Introduction: Misoprostol is commonly used prostaglandin to induce labor. Several recent trials have confirmed that misoprostol is highly effective. Overall caesarean delivery rates appear to be reduced. Concern remains regarding increased rates of uterine hyperstimulation and meconium-stained amniotic fluid, although data on perinatal outcome has been reassuring.

Objectives: To evaluate the efficacy and safety of vaginal misoprostol for induction of labor.

Material and Methods: A retrospective study was performed on 60 women undergoing induction of labor with misoprostol, between January 2008 and February 2009. The dose of misoprostol was 25mg intravaginally every 12h.

Results: Average age at time of pregnancy was 29.97 years (17-43). Sixty seven percent of the women were nullipara. Average gestational age was 40.38 weeks (36-41). The indication for labor induction was gestational age superior to 41 weeks in 46 women, maternal indication in 10 and other indication in 4. The average score of induction was 2.83 (0-6). The mean induction vaginal delivery time interval was 18 hours (6-39). The median number of doses for misoprostol use was 1.4. Seventy five percent of mothers had a vaginal delivery and 25% had a caesarean delivery. There was only one case of tachysystole (1.7%). The median weight at birth was 3432.7g and all had good Apgar Scores. Three babies were admitted at Neonatal Intensive Care Unit.

Conclusions: The Results of our study demonstrate that misoprostol use for labor induction appears to be safe with low complications and low incidence of caesarean section delivery.

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Safety profile of intravaginal isosorbide mononitrate for cervical ripening before the induction of labor at term

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Aim: To investigate the safety profile of intravaginal isosorbide mononitrate (IMN) for cervical ripening in outpatient use.

Material and method: We prospectively enrolled 64 primiparas with singleton pregnancy, cephalic presentation, at least 37 weeks of gestation, normal admission cardiotocography and a modified Bishop score $\leq 6$. They received 40mg of IMN into the posterior vaginal fornix, after sixteen hours the cervical score were reassessed and a second dose of 40mg IMN was administered if Bishop score was still $\leq 6$. Next evaluation was scheduled at 24 hours after the first dose. Second dose was withhold in case of membranes rupture, vaginal bleeding, Bishop score $>6$ or onset of labor. Safety outcomes were assessed by cardiotocography, performed initially and at 30 min, 6, 15.5, 17 and 24 hours, blood pressure and heart rate monitoring initially and at 1, 2, 6, 10, 16, 20, 24 and 28 hours. The incidence of maternal side effects such as headache, dizziness, somnolence, nausea and vomiting was noted and the intensity recorded on a visual analog scale (VAS).

Results: We found no abnormal fetal heart rate patterns. The most often occurring side effect was headache 43/64 with a median VAS score of 6, followed by nausea 37/64. There were no cases of tachycardia or hypotension that required treatment. 50% of women needed 2 doses for cervical ripening and in six (9%) cases we failed to rise the Bishop score $>6$.

Conclusion: Our data shows that IMN is safe to administer in outpatients for cervical ripening prior to induction of labor at term.

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Predisposing factors for oxytocin augmentation as the first intervention during labor

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Aim: We examined predisposing factors for oxytocin augmentation as the first intervention among several administered during labor.

Methods: The ProGeb-Study in Lower Saxony, Germany, included 3963 low-risk women with a singleton fetus in cephalic presentation. Intervals from onset of labor to the first intervention were analyzed by Cox regression, examining oxytocin, amniotomy and epidural analgesia as competing risks. Demographic, fetal, risk-associated and induction-related factors were included as covariates. 1322 women were excluded as they had no documented interventions during labor.

Results: For 510 nulliparae and 299 multiparae oxytocin augmentation occurred as their first intervention after median periods of 10.3h and 8.8h respectively. Other women received epidural analgesia (n=769) or amniotomy (n=1063) as the first intervention.

In nulliparae, PROM and induction with oxytocin or amniotomy were associated with a shorter interval from onset of labor to the start of intrapartum oxytocin augmentation.

In third parae among the multiparae, increased neonatal length, lower birth weight, meconium stained liquor, PROM and different modes of induction were associated with a shorter interval from onset of labor until the start of oxytocin. Other factors such as risk-associated factors showed no significant associations.

Discussion: Oxytocin as the intervention of first choice is mainly chosen for women who have already experienced induction of labor, PROM or meconium stained liquor. Oxytocin augmentation is obviously not the intervention of first choice for women suffering from risk associated factors, but is favoured for women who need to give birth fairly speedily due to fetal symptoms.

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The role of the maternal plasma Total Antioxidant levels in postterm pregnancy etiology

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Objective: To investigate the role of oxidative stress in postterm pregnancy etiology measuring the Total Antioxidant Status (TAS)

Material-Methods: The level of TAS was measured in maternal plasma of 50 cases that were followed in our antenatal care unit and still haven’t delivered in the 41st week of their pregnancy. Those cases were included in the study group. 33 cases in which the maternal plasma TAS levels were measured during the 37-38th week of the pregnancy in which the delivery spontaneously occurred before 40th week of pregnancy were considered as control group and the TAS values were compared between the groups.

Results: The mean age of the groups were similar (26.5±5.6 vs. 25.03±3.8) between the groups, but mean gravidity and parity were significantly higher in the study group (p=0.48 and p=0.48 respectively). The mean gestational age at birth was 41.2±0.22 weeks in the study group and 38.5±4.1 weeks in the control group.

When mean serum TAS values were compared between two groups, they were found to be 1.64±0.12mmol/L and 1.78±0.06mmol/L in subjects and control groups respectively, with a significant difference (p<0.001).

Conclusion: According to the findings of present study, oxidative stress status during pregnancy can taken a role in postterm pregnancy and total antioxidant status levels may be clinically useful in the prediction or diagnosis of postterm pregnancy.

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Does pregnancy influence on pharmacokinetics of ceftriaxone, cefazolin and gentamicin in elective caesarean section?

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Objectives: To study the effect of pregnancy on postoperative ceftriaxone, cefazolin and gentamicin elimination rate constant, half-life, volume of distribution and systemic clearance.

Methods: 54 patients undergoing caesarean section and 12 undergoing gynaecological surgery were given intravenous dose of ceftriaxone, cefazolin or gentamicin immediately before the operation, for chemoprophylaxis. The levels of antibiotics were measured in blood plasma, amniotic fluid and umbilical cord blood plasma by HPLC for the cephalosporins and by fluorescence polarization immunoassay for gentamicin. Pharmacokinetic parameters were estimated using a one-compartment model.

Results: Pregnancy significantly influenced the pharmacokinetics of ceftriaxone and gentamicin, but not that of cefazolin. Ceftriaxone constant of elimination decreased statistically significantly in caesarean-sectioned women relative to the non-pregnant subjects (ke=0.1817±0.0454 non-pregnant patients; ke=0.1109±0.0416 pregnant patients). Gentamicin constant of elimination increased significantly in caesarean-sectioned women relative to the controls (ke=0.3198±0.0943-non-pregnant patients; ke=0.4127±0.0736 pregnant patients). The concentration of antibiotics in umbilical cord blood were higher (ceftriaxone-29.2±26.1mg/L; cefazolin-54±24.9mg/L; gentamicin-6.80±2.17mg/L) whereas they were substantially lower in amniotic fluid than in maternal plasma (ceftriaxone-1.54±2.10mg/L; cefazolin-6.80±3.78mg/L; gentamicin-2.09±1.26mg/L). Six hours after antibiotic administration, only the cefazolin concentrations exceeded the MIC for sensitive bacteria both in pregnant and in non-pregnant patients.

Conclusion: Analysis of the pharmacokinetic data suggests that a single-dose of cefazolin may well be the optimal preoperative prophylactic treatment for obstetrical and gynaecological surgical procedures.

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Oxytocin use during labor

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Objectives: Verify the frequency of oxytocin use during labor; identify factors that favor its use; assess the occurrence of complications consequent to oxytocin. Methodology: Descriptive retrospective study. Variables studied: maternal conditions, oxytocin use, obstetric examination, duration of 1st labor period, type of birth, fetal Result and the occurrence of complications. Results: A total of 316 births was studied. Two groups were identified: Group I – received oxytocin and Group II - did not receive oxytocin in the active phase of labor.

<table>
<thead>
<tr>
<th>Group</th>
<th>I</th>
<th>II</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients</td>
<td>205 (65%)</td>
<td>111 (35%)</td>
</tr>
<tr>
<td>Parity (p=0.010)</td>
<td>104 primiparas 101 multiparas</td>
<td>39 primiparas 69 multiparas</td>
</tr>
<tr>
<td>Average Age (p=0.001)</td>
<td>23 years</td>
<td>27 years</td>
</tr>
<tr>
<td>Initial cervixl (p=0.484)</td>
<td>3.0cm</td>
<td>2.0cm</td>
</tr>
<tr>
<td>Average duration TP (p=0.130)</td>
<td>7h</td>
<td>6h</td>
</tr>
<tr>
<td>Type of birth (p=1.000)</td>
<td>I) 165 (80.5%) vaginal 40 (19.5%) caesarean sections</td>
<td>II) 89 (80%) vaginal 22 (20%) caesarean sections</td>
</tr>
<tr>
<td>Peso Médio do RN (p=0.046)</td>
<td>3057g</td>
<td>3183g</td>
</tr>
<tr>
<td>NB Apgar (p=0.575)</td>
<td>13 cases of hypoxia</td>
<td>12 cases of hypoxia</td>
</tr>
</tbody>
</table>

The patients in group I presented average 7.0cm cervical dilation when oxytocin was administered. At that moment the waters were broken artificially in 92, broke spontaneously in 64 and were intact in only one patient. The uterine activity was adequate in 121 (59%) of the patients and inadequate in 85 (41%). There was no hypersystolia or uterine rupture. Conclusion: The use of oxytocin was frequent and more common among primiparas. Oxytocin did not cause mother-fetus complications, but did not reduce the dilation period or increase the rate of vaginal births.

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The relationship between the onset of labor mechanisms and the hemostatic system

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The relationship between onset of labor and the hemostatic system was evaluated in 38 pregnant women.

The hemostatic system consists of blood coagulation, Kinin-Kallikrein system, the fibrinolytic system, and platelet function. The most prominent changes take place in the Kinin-Kallikrein system. After onset of labor, prekallikrein decreases rapidly which may trigger changes in blood coagulation and the fibrinolytic system. Platelet hemostatic capacity (PHC) was also measured using the PFA-100(Platelet function analyzer) system. Closure time (CT) were shorter during pregnancy, compared to the onset of labor. At the same time a slight increase in FDP (fibrin degenerative Product) was also seen.

While FDP increased, Platelet aggregation decreased, which seems to suggest FDP inhibit platelet aggregation.

In this manner, these three system (Kinink-Kallikrein, Blood coagulation, Fibrinolytic system) and platelet-aggregation are closely interrelated, possibly affecting uterine contractility during pregnancy and the onset of labor.

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Pelvic arterial embolization for management of postpartum hemorrhage

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Objectives: An increasing number of cases with massive obstetric hemorrhage have been managed with pelvic artery embolization (PAE). The purpose of this retrospective study is to evaluate the efficacy and safety of PAE. Methods Data were collected, from clinical records at our institution, on all patients with postpartum hemorrhage managed with PAE between April 2002 and February 2009. Results: During the study period, a total of 17 patients underwent PAE to control massive postpartum hemorrhage. Among those patients, 8 cases had a vaginal delivery and 9 cases had a caesarean section. The indications for PAE include uterine atony (6 cases), placenta previa (5), uterine rupture (2), and vaginal wall hematoma (2). Disseminated intravascular coagulation developed in 11 cases and all required blood transfusion. The mean time between delivery and PAE was 5.6 hours. The average procedure time for PAE was 1.4 hours. The uterine artery was the most frequently embolized vessel (in 11 patients). The average blood loss was 3519ml. Optimal hemostasis was achieved at the initial procedure in all cases but two, who required an additional embolization. Three cases underwent hysterectomy. No severe complications were observed. Among cases in which the uterus was preserved and follow-up information was available, one patient became pregnant and gave birth to a healthy baby at term.

Conclusions: PAE, particularly uterine artery embolization, is an effective, safe method to control massive postpartum hemorrhage, providing the patients with sufficient opportunity to maintain reproductive ability.

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Controversies in hybrid banking: attitudes of Swiss public umbilical cord blood donors towards private and public banking

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Background: Public umbilical cord blood (UCB) has become an alternative stem cell source for allogeneic stem cell transplantation. The potential use of autologous UCB from private banks is a matter of debate. Because of the limited resources of public inventories, a discussion on “hybrid” public and private UCB banking has evolved. We aimed to explore the attitudes of the donating parents towards public and private UCB banking.

Study design: A questionnaire was sent to the most recent 621 public UCB donors including items regarding satisfaction with recruitment process, the need for a re-consent before release of the UCB unit for transplantation, and the donor’s views on public banking, private banking and UCB research.

Results: Forty-eight percent of the questionnaires were returned, and 16% were lost for mail contact. Twenty-seven percent had never heard about private UCB banking whereas 34% discussed both options. Nearly 70% of donors decided for public banking due to altruism and the high costs of private banking. Eighty-one percent of our public UCB donors stated that they don’t need a re-consent before UCB release for stem cell transplantation. In case of sample rejection 53.5% wanted to know details about the potential research project. Nine percent would not consent.

Conclusion: Almost all donors would choose public banking again due to altruism and the high costs of private banking. Shortly after donation, mail contact with former UCB donors was difficult to obtain. This might be a relevant issue in any sequential hybrid banking model.

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Human recombinant activated factor VII in treatment of massive obstetric haemorrhage caused by uterine atony

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Objective: Massive obstetric hemorrhage is the most common cause of maternal morbidity and mortality. Although recombinant activated factor VII (rFVIIa) is not registered for the treatment of this condition, it has been found useful in small case series. The aim of this study is to show our experience with rFVIIa in the treatment of patients with massive obstetric hemorrhage.

Materials and Methods: The study encompassed 3 patients with primary postpartum hemorrhage caused by uterine atony alone treated with rFVIIa. None of them had any comorbidity.

Results: All patients were treated with symptomatic and substitutional medical therapy, and were given 90 mcg/kg rFVIIa which resulted in cessation of the bleeding. The first patient was delivered by caesarean, followed by hysterectomy and internal iliac artery ligation. Due to persistent bleeding rFVIIa was given 25 hours after delivery. The second patient was delivered vaginally, and underwent revision of vaginal and cervical lacerations, uterine curettage and tamponade. The drug was given 5 hours after delivery. Encouraged with those results, rFVIIa was given in the third case within the 2 hours after delivery.

Conclusion: The administration of rFVIIa should be considered as a treatment option in cases of massive obstetrics hemorrhage, following detailed revision of surgical hemostasis. It might be particularly useful in those cases where the preservation of the uterus is desired. The best timing of administration needs yet to be established.

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B-Lynch sutures for massive postpartum hemorrhage at caesarean section

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Introduction: Postpartum hemorrhage remains one of the major causes of maternal morbidity and mortality throughout the world. Uterine atony is the most common cause and is primarily managed medically, but surgical procedures including hysterectomy, may be necessary. B-Lynch is a uterine compression suture technique first described in 1997. Being a conservative treatment, it potentially preserves the patient’s fertility. CLINICAL CASES: Three young (19 to 23 years-old) healthy primigravida underwent caesarean section at term due to labor arrest, cephalopelvic disproportion and failed induction of labor. These were singleton uneventful pregnancies and the newborns weighted 3,630 to 3,860g. Postpartum massive hemorrhage was identified intraoperatively and besides uterine massage, pharmacologic treatment was undertaken in a stepwise manner: intravenous oxytocin (plus intramyometrial injection in two cases), intravenous sulprostone (plus intramyometrial administration in one case) and rectal misoprostol in two cases. As it was not effective, B-Lynch sutures were performed and hemorrhage control was achieved. All required blood transfusion and in one case a coagulopathy developed with the need for several blood derivatives. The three women were discharged within the first postoperative week and were clinically well several months after the delivery. Hysteroscopy was performed and showed a normal uterine cavity.

Discussion: B-Lynch sutures permitted uterus preservation, which is particularly important considering the patients were young and primigravida. As the procedures were undertaken less than two years ago, there have not been pregnancy attempts yet, therefore their current fertility, though theoretically not affected, remains unknown.

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Postpartum severe hemorrhages in our clinic – etiology and attitude

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Postpartum hemorrhages (PH) is the leading cause of maternal mortality in Romania. We conducted a retrospective study over three years in our Clinic. There were reported 6.52% cases of PH after vaginal delivery and 13.37% cases after c-sections. The more frequent possible causes of PH after vaginal deliveries were uterine atony in 55 patients and retained placenta in 36 patients. Among the c-sections deliveries complicated by PH the causes was uterine atony in 33.33%, The anesthetic methods in the c-section deliveries were - general anesthesia and orotracheal intubation 93.73%, spinal anesthesia, epidural anesthesia, and combined anesthesia for rest. PH Management after vaginal delivery consisted in: manual removal of retained products, oxytocin/Ergometrine/Ergonovine maleat administration, curettage, administration of red blood cell concentrate was required. In case of PH after c-section the following measures and procedures were taken: fundal massage, oxytocin and Ergometrine/Ergonovine maleat administration, total hysterectomy in 1.47% cases, subtotal hysterectomy in 1.18% cases, uterine vessel ligation in 2.06% and other procedures in 2.36% cases.

Conclusions: we found a significant increase in the incidence of PH after c-section from 9.85% in 2006 to 16.15% in 2008, and a lower, insignificant increase for this complication in the case of vaginal deliveries – from 6.02% in 2006 to 7.1% in 2008. The most common cause reported in 2008 for the postpartum hemorrhages was uterine atony without another obvious causes nos 61.94% in 2008, compared to 31.86% in 2006 and only 6.2% in 2007.

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Retrospective analysis of 57 cases with life threatening peripartal hemorrhage treated with recombinated activated factor seven (rFVIIa)

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Objectives: Assess the benefit of rFVIIa administration in the treatment of severe peripartal hemorrhage.

Study Design: We analyzed 57 cases of severe peripartal hemorrhage in which rFVIIa was used in the treatment between January 1998 and December 2008. The estimated blood loss was more than 2 000ml in each case.

Results: 56 women survived. The median time from onset of bleeding event to administration of rFVIIa was 240 minutes. The mean of first dose was 100µg/kg, the second and the third dose was used in 18 (35%) and 5 (9%) cases respectively 5(9%). Hysterectomy was carried out in 32 (68%) cases mainly before rFVIIa administration. In 11 (34%) cases hysterectomy did not stopped the bleeding and surgical revision of abdominal cavity was necessary. The use of rFVIIa statistically significantly decreased (p<0.001) the necessity of blood components (erytrocytes, plasma, etc.) replacement. We noted that the more frequent use of rFVIIa before the surgical intervention in the last 3 years rapidly decreased the rate of hysterectomy in hypotonic cause of postpartal hemorrhage. We have no encountered any thrombotic events with administration of rFVIIa.

Conclusions: rFVIIa is an effective agent in the treatment of life threatening peripartal hemorrhage and should be an integral part of the management of this serious unexpected event. This “off label” indication helps to save not only life of the women but could help to save the woman’s fertility.

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Anthropometric measures of head-shoulder-ratio in infants of women suffering from gestational diabetes and of controls with normal glucose tolerance

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Background and Aims: Differences in the head-shoulder-ratio between infants of diabetic and non-diabetic mothers have been reported. This may explain the supposed propensity for shoulder dystocia in the diabetic population and thus account for a higher percentage of caesarean sections. A more recent study with a small sample size, however, has shown the converse. Therefore our specific aim was to investigate in a large number of patients whether anthropometric measurements differ between infants of mothers with normal glucose tolerance and mothers suffering from gestational diabetes.

Methods: This is a case control study. A chart review of all patients of the Division of Obstetrics and Feto-Maternal Medicine of the Medical University of Vienna suffering from gestational diabetes who gave birth between January 1st, 2004 and June 30th, 2008 was carried out. Controls were non-diabetic mothers matched for maternal age, gestational age and birth weight. Student's t-Tests were used to compare parameters between cases and controls. P<0.05 was considered significant.

Results: 768 patients in each group were included. The head-shoulder-ratio did not differ significantly between cases and controls (P 0.14). A secondary analysis of macrosomic neonates (birth-weight >4000g) was carried out and again the head-shoulder ratio did not differ significantly between infants of diabetic and non-diabetic mothers (P 0.23).

Conclusion: Anthropometric measurements of neonates of mothers with gestational diabetes do not differ from infants of non-diabetic mothers thus allowing the same management of delivery in patients with controlled diabetes as in patients with normal glucose tolerance.

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The evaluation of the delivery route and outcomes of 221 Macrosomic (birth weight ≥4,000g) fetuses

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Objective: To evaluate the perinatal outcome in a series of macrosomic fetuses according to the mode of delivery.

Materials-Methods: Maternal and neonatal records of infants with birth weights of at least 4000g were identified during the 5-year period. Outcome variables included the mode of delivery and incidence of perinatal complications.

Results: 221 cases were analyzed. The mean gestational age was 40.13±1.07 weeks, mean birth weight 4,231±214g. 32.7% of our patients were nulliparous and 20 of patients (9%) were diagnosed to have DM. 140 of patients (63.3%) delivered vaginally. The indications of caesarean section were; 39.5% non-progressive labor/cephalopelvic disproportion, 13.6% fetal distress, and 13.6% elective for suspected fetal macrosomia respectively. Shoulder dystocia occurred with an incidence of 10.7% in vaginal deliveries for macrosomia. There were five cases of brachial plexus injury and/or clavicular fracture in vaginal delivery and none in caesarean. In all of those 5 cases ultrasonographically estimated fetal birth weight was below 4000g prior of the delivery. 6.4% neonatal respiratuar problems detected in vaginal delivery and only one in caesarean. 12 of vaginal deliveries had severe perineal trauma and vaginal lacerations were noticed. The number of newborns in weight ≥4500g were 31 (14%) and 16 of these were born via vaginal route and brachial plexus injury appeared in only one.

Conclusion: In cases having predictive fetal weight more than 4000g, the opinion that indicates birth with the absolute caesarean is obligatory should be reexamined and the chance of vaginal delivery should be considered.

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Risk in vaginal delivery for LGA fetuses

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In this study are included fetuses large for their gestational age with birth weight over 4,000gr which were delivered in the period from 2005 till 2008 on our clinic. 994 deliveries in total were studied, from which 248 or 25% were delivered with caesarean section, and the rest were delivered vaginally. Apgar score values in the first 5 minutes and post partal pH values were examined in all deliveries. Analysis showed that there is no significant difference in the way the delivery was made, C.S. or vaginally, respectively. This concludes that there is no significant risk correlating morbidity or mortality in the way of the delivery of LGA fetuses, only if there is no other additional risk concerning the pregnancy.

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The delivery of the macrosomic fetus

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Introduction: In current obstetrics, the macrosomic fetus represents a frequent clinical challenge. The delivery of macrosomic infant has potentially serious consequences for the infant and the mother. The objective of this study was to determine the influence of spontaneous versus elective delivery (induction or caesarean section) of suspected fetal macrosomia on some of maternal and fetal complications.

Materials and methods: Retrospective analysis of medical records of all women who had delivered a macrosomic infant (fetal birth weight more than 4,000g) at our department between January 2006 and December 2008 was performed.

Results: The Results will be presented later and will include the rate of perineotomy, perineal trauma, postpartum haemorrhage and fetal injury.

Conclusion: Delivery of a macrosomic fetus requires considered attention by an experienced obstetrician.

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Fetal macrosomia: Obstetric outcome in low-risk women

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Objective: To determine macrosomia prevalence and analyze obstetric outcome associated with delivery of macrosomic fetuses in low-risk women.

Methodology: Through a case-control study, 2,574 medical records were analyzed among patients who delivered macrosomic fetuses (≥4,000g) comparing with delivery of normosomic control group (2,500-3,999g), taking place at the Associação Pró-Matre, from February 2005 to March 2007. Cases were further divided into two groups according to birth weight: 4,000 - 4,499g (G1) and ≥4,500g (G2). In both groups, data were subjected to univariate statistics, and to assess the independence of factors associated with macrosomia.

Results: The final prevalence obtained for macrosomia was 6.65%±1.23 out of 19,574 deliveries. Obstetric variables associated to macrosomia were: caesarean delivery (G1: OR=2.28 [1.93-2.70] e G2: OR=3.13 [2.20-4.45]) and shoulder dystocia (G1: OR=3.36 [1.36-9.27] e G2: OR=7.57 [2.10-26.29]) for both groups, and fetal distress only for group ≥4,500g (OR=1.81 [1.12-2.84]). Postpartum hemorrhage and severe perineal laceration (third and fourth degrees) did not show association with fetal macrosomia.

Conclusion: Prevalence obtained for macrosomia in the present study was in agreement with Brazilian data. However, the fact that it concerns to low-risk pregnancies, probably being determinate by factors as obesity and excessive weight gain, must be taken into consideration. Nonetheless the present Result suggests that delivery of macrosomic fetuses is associated with obstetric adverse outcomes increasing across varying birth weight thresholds.

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Epidural analgesia as the first intervention during labor is associated with a risk profile in pregnant women

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Aim: We examined factors which predict epidural analgesia as the first intervention among several administered during labor.

Methods
Intervals from onset of labor to the first intervention were analyzed by Cox regression, examining epidural analgesia, amniotomy and oxytocin in 3963 low-risk women. 1322 women were excluded as they had no intervention from onset of labor onwards. Demographic, fetal, risk-associated and induction-related factors were included as covariates.

Results: In 580 nulliparae and 189 multiparae the cascade of interventions started with epidural analgesia, in most cases followed by oxytocin (np:59.1%; mp:43.9%) or amniotomy (np:20.5%; mp:22.2%). Other women received amniotomy (n=1063) or oxytocin augmentation (n=809) as a first intervention. In nulliparae risk-associated factors such as smoking, VBAC-status, diabetes mellitus, PROM, no prolonged pushing due to previous disease, but also no documented risk factors (54.3%) were associated with a shorter interval from onset of labor to epidural analgesia. Fetal predictors such as head circumference, birth weight and length were also associated with the timing of an epidural. In multiparae, advanced maternal age, meconium stained liquor and PROM represented risk factors for epidural analgesia as the first intervention. Induced women experienced an earlier start of an epidural compared to women without an induction. Other factors showed no significant associations.

Discussion: Demographic, risk-associated, fetal and induction-related factors were significantly associated with epidural analgesia as the first intervention in nulliparae and to a less extent in multiparae. More than half of the nullipare receiving epidural analgesia first had no risk profile in their history.

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Use of spinal anaesthesia and nacrotic analgesia to facilitate external cephalic: a double-blinded randomized controlled study

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Objective: To investigate whether spinal anaesthesia (SA) or Remifentanil could improve success rate of external cephalic version (ECV).

Methods: Patients who had an uncomplicated singleton breech-presenting pregnancy undergoing ECV were randomized to have either (1) SA, (2) Remifentanil iv infusion, or (3) placebo, with stratification according to parity. Both patients and the operators were blinded to the randomisation. ECV was then conducted under a standard protocol with hexaprenaline as tocolysis. Patients’ pain experience during ECV was assessed using visual analog scale (0-10). Success rate was then compared between the 3 groups.

Results: 60 nulliparous and 60 multiparous patients were recruited (20 patients in each group respectively). Overall, SA Group had a higher success rate than Remifentanil Group and Placebo Group (87.5% vs. 57.5% and 62.5%; p=0.008) but the latter two were not different from each other. After stratifying according to parity, Group A still had a higher success rate among nulliparous (80% vs. 45% and 55%) as well as among multiparous (95% vs. 70% and 70%). The median pain score was also lower in Group A than in the other two groups (0 vs. 5 and 5; p<0.001).

Conclusion: SA but not Remifentanil improved the success rate of ECV and reduced the pain experience during the procedure.

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Effects of epidural analgesia in labor on newborns

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The application of the epidural analgesia (EA), during labor has an effect on a physiological status of a mother as well as of a newborn. The goal is to examine effects of the EA on a newborn. Retrospective analysis included 6398 patient newborns, born during the 2003. First group is made out of 455 newborns born in EA. Control group is out of 5943 without EA.

Parameters were sex, gestational age, body mass, Apgar score.

Average age of patients in the first group was 30.5±4.5 years. EA was used in most cases in primiparas (66.8%) and multiparas (26.2%). In 86.6% of deliveries no obstetric interventions were made. In study group 4.6% were delivered by VE, much higher than in control group. Newborns in the first group were in the full term. Gestational age was 39.0±1.0, body mass of 3,448±412 grams. Newborns from the EA have significantly higher Apgar score than ones from the control group. Lower pH values were seen in the group of newborns that were delivered by SC or the VE. Relation between the duration of the delivery and pH levels was not established. Perinatal morbidity shows that the level of HIE is lower in the EA group 1.1% vs. 2.8%. Other parameters did not show the difference.

Conclusions: Application of the EA during delivery doesn't increase the incidence of early perinatal morbidity. Proper appliance of the EA during delivery unwanted effects are of no significance, clinically worthless, so the newborns are in good health and adaptability at birth.
The course and the outcome of deliveries conducted in the epidural anaesthesia

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Epidural anaesthesia (EA) is the most efficient way of pain reduction and its total relief during delivery. Objective was to monitor the course and the outcome of the delivery in epidural anaesthesia. Investigated group was made of 794 patients with delivery in EA, during 2004, and control group 5566 patients that had deliveries without it. All of the pregnant women that gave birth vaginally in EA were significantly older than those in the control group. Delivery period was shorter in primipara group with EA, but was much longer in multiparas that gave birth vaginally, and in all other patients who had a SC in EA. Multiparas in EA had a significantly larger number of vaginal mucosa and cervical ruptures, defect placentas and post delivery bleedings. Larger number of deliveries in EA had an obstetric instrumental interventions compared with those in the control group. There was a larger number of transfusions in the group of primiparas in EA that gave vaginal birth, and also with the multiparas who had a SC than in the similar sections of the control group (3.6% and 50% vs. 1.4% and 1.7%). Apgar score of the newborns was statistically higher in the investigated group, except with primiparas, where the duration of the hospital treatment was longer. The pain relief and comfort of labor was enormously better. Considering all the aspects, in our opinion, with an adequate preparations, determination and, respecting delivery protocols, constant monitoring, the delivery in EA has its significant place in the up to date obstetrics' practice.

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Route of delivery after stress urinary incontinence (SUI) tension-free tape surgery

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Background: Stress urinary incontinence (SUI) is the most common type of urinary incontinence in women under age 60 and it is found in 12.4% of 40 year old women. Due to its good Results and low risks, surgical correction is now offered to women of childbearing age. Given the lack of data, it is difficult to counsel patients on their expected continence status with future pregnancy and the effect of route of delivery.

Objective: Study the route of delivery in patients who have undergone tension-free tape surgery.

Materials and Methods: Review of the published cases of pregnancy in women with previous tension-free tape surgery, and a case occurred in our hospital.

Results: We found 11 cases who finished by caesarean section and 14 by vaginal delivery. The proportions of recurrence were 9% for the CS and 14% for vaginal delivery. We applied a Newcombe test obtaining a CI95% -0.255 to 0.32, which demonstrates lack of significance of the difference and an evident lack of power. Our case is a 39 year old gravida 3 para 1 ectopic pregnancy 1 who became pregnant 2 years after undergoing TVT-O and delivered vaginally. The patient had no recurrence of SUI during pregnancy and remained continent postpartum.

Conclusion: Vaginal delivery is a suitable route of delivery for women who had undergone tension-free tape surgery in absence of other obstetric indications for caesarean section.

We need more data to be able to elaborate clear guidelines for the management of this kind of patients.

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Perinatal outcome of term pregnancies with meconium-stained amniotic fluid

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Purpose: The purpose of this study was to compare the obstetric and perinatal outcome between two groups which complicated with or without meconium staining of amniotic fluid (MSAF) at term birth in one-year consecutive population at our delivery unit.

Methods: Pregnancy complication including fetal distress, intrauterine growth retardation, oligohydramnios, hydramnios and preeclampsia between the two groups were retrospectively documented by review of medical record. To evaluate the perinatal outcome, apgar score at 1min and 5min, and umbilical artery blood gas analysis were also analyzed. Student T test and chi square test were used for statistic analysis.

Results: The study population was consisted of 687 full-term neonates with presence (n=89) and absence (n=598) of MSAF. Gestational age at delivery was significantly higher in MSAF group (p<0.001). Although the fetal acidemia (umbilical artery blood pH<7.0) was significantly higher in MSAF group (3.4% vs. 1.0%, p<0.01), the metabolic acidemia (base deficit >12.0mEq/L) was not increased. The incidence of fetal distress was also increased in the MSAF group (4.5% vs. 1.0%, p=0.03). However there was no significant difference in 1min and 5min apgar score.

Conclusion: Although MSAF is associated with the risk of fetal distress and fetal acidemia, the metabolic acidemia and low apgar score at 5minutes was not significantly increased compared with clear amniotic fluid group. Delivery of pregnancy with MSAF should be managed under the careful fetal heart rate monitoring.

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**Regression of the cervix after vaginal delivery**

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Introduction: At the time of birth the conjunctive tissue of the uterine cervix and body undergo enzymatic action from collagenase, leading to a reorganization of the collagen fibrils and preparing the cervix for the birth. The average time needed to remodel the cervix and body should be determined because they can be predictors of puerperal complications.

Objective: Define the average time of cervix impermeability assessed by the digital vaginal touch in post natural birth.

Casuistic and Methods: Thirty primiparas were assessed (age: 18 to 28, average 22 years) monitored through the pre-natal period, that did not present co-morbidity factors and evolved without complications during natural birth. The digital vaginal touch was used, assessed by a single observer on the 1st, 4th, 7th, 10th and 14th day post vaginal delivery. The cervix was considered permeable when the orifice was greater or equal to a finger tip.

Results: All the 30 patients presented permeable cervix until the 4th day post partum. On the 7th day post vaginal delivery, 6 patients (20%) presented cervix impermeable to vaginal touch, on the 10th day post vaginal delivery, 21 patients (70%) presented impermeable cervix and on the 14th day vaginal delivery the last 3 patients (10%) presented impermeable cervix.

Conclusion: In healthy patients submitted to natural birth the cervix was impermeable until the 14th day post partum. These data are interesting in the assessments of puerperas that have complications and cervix permeability remaining after the 14th puerperal day.

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Influence of overdueness on the type of labor and the neonatal Result

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Introduction: Progressive increase has been observed in caesarian section rates, with increase in maternal morbimortality, without benefits to the newborns. Overdueness is a common clinical entity and may be associated with the birth process and alterations in the fetus well-being.

Objectives: Assess the influence of overdueness on the type of labor and the neonatal Result.

Methodology: Retrospective study of births at term and overdue birth that occurred from May to December 2007 at the Pouso Alegre University Hospital, Brazil. The following variables were assessed: type of birth and Apgar of the 1st and 5th minutes. Pathological obstetric, clinical, surgical cases and elective caesarian sections were excluded. Two groups were identified: GI- term gestation and GII - overdue gestation.

Results: A total of 804 births were included in the study, 470 term gestations and 334 overdue gestations. In GI there were 346 (73.6%) vaginal deliveries and 124 (26.4%) caesarean sections while in GII there were 220 (64.9%) vaginal deliveries and 114 (34.1%) caesarean sections (p=0.018). In GI 24 indices were observed of Apgar 1st<7 and in GII 29 cases (P=0.108). In GI 11 indices of 5th<7 were detected and in GII 8 cases (p=0.934).

Conclusion: Overdueness increased the rate of caesarean sections but did not interfere in neonatal hypoxia.

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Acupuncture treatment to reduce labor induction for prolonged pregnancy

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Prolonged pregnancy represents a frequent indication for labor induction. Labor induction is related to higher risk of caesarean section and operative delivery. Traditional Chinese Medicine (MTC) advised the use of acupuncture as a pre-birth treatment starting from the 36th week in order to promote the ripening of the cervix and to relax the mother. In the last 5 years acupuncture some studies applied as pre-birth treatment and in the case of rupture of the membranes reporting that acupuncture was able to reduce the first and second stage of labor.

In the present, case-control study for each women receiving acupuncture a women at similar gestational age, similar Bishop score and similar parity was chosen. Exclusion criteria were considered maternal or fetal disease and any pregnancy complications. After obtaining oral consent each women receiving acupuncture was submitted to a session twice a week until the 40+5 week. Acupuncture group showed a significant lower rate of induction for prolonged pregnancy (10% vs. 46%; p<0.02) and a trend to lower duration of the first stage of labor. The duration of the second stage of labor and the rate of caesarean section do not differed between groups.

The promising Results of the present study should stimulate authors to apply acupuncture at term to avoid pharmacological induction of labor.

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Use of complementary and alternative medicine in obstetrics - a survey from North Rhine-Westphalia, Germany

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Background: Our earlier study on the use of complementary and alternative medicine (CAM) methods showed that acupuncture, homoeopathy and aromatherapy are used in the vast majority of German obstetrical departments mainly under the accountability of midwives. This study, however, did not assess the indications in which these methods are used. In order to elucidate the area we underwent this study.

Methods: All obstetrical departments in North Rhine-Westphalia were identified and sent a questionnaire designed to assess which CAM methods are used in which situations during childbirth. SPSS software was used for statistical analyzes (Spearman’s bivariate correlation, cross-tabulation, and Pearson’s Chi-square test).

Results: Questionnaires were returned by 71.2% (141/198) of departments identified.

Conclusions: CAM methods are widely used in German obstetrics, despite a lack of evidence of their effectiveness. Efficacy, side effects and consequences of CAM use should be assessed using the mandatory German quality assurance measures and birth surveys. CAM use elsewhere also merits further study.

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Midwifery orientating documentation tool to guide the care of women during the early labor period

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Background: Midwives working in midwife-led units in hospitals meet several challenges in the development of a new working culture, which enables them to maximize women-centered care and support normal birth. They need new and extended skills to attend laboring women. The purposes of this study are to develop a tool to structure and reflect midwifery care. We aim to give guidance in improving autonomous care, support intra-professional collaboration, support women-centered care and shared decision making.

Method: This prospective control study is based on a triangulation of qualitative and quantitative methods. In a first step medical records, semi-structured interviews with midwives (n=11), an interdisciplinary working group and literature review were performed and analyzed. The product of this first step was the intervention instrument, the Midwifery Orientating Documentation (MOD). This instrument was introduced to the midwifery team during two teaching units in February 2008. Beginning in December 2009 we will analyze and compare data from two groups (intervention- and control hospital; n=133 each). Primary endpoint is reasons for referral from MLU to consultant care. Additionally we analyze the quality of the documentation for further development purposes.

Discussion: For midwifery as a complex task it is necessary to describe and to record the care provided. The development of assessment instruments and midwifery diagnoses particularly for emotional and psycho-social aspects of care and a transparent care process are vital for the defining of competence and responsibility domains.

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Preferences of pregnant women comparing midwife-led and consultant-led care
- First Results from a cost-benefit analysis

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Background: Arising expenses in the social security system financed through contributions as well as a lack of evidence based practice are obvious in German health system. Therefore the legal framework requires health economic studies.

Regarding maternal health, the caesarean rate is increasing rapidly in Germany from 18% in 1995 to 30% in 2006 (destatis 2007). Apart from detrimental health effects for women and children, rising interventions rates cause increasing costs. The concept of midwife-led care is discussed as an option to decrease these rates and to cause more continuity of care (Hatem 2008).

Summary: The cost-benefit analysis is designed as a prospectively controlled study (n=750) and compares midwife-led care with consultant-led care. The expression of individual preferences by childbearing women and the consideration of savings are defined as benefit. Costs were derived from activity-based-costing.

Preferences are measured by contingent valuation, in detail with a closed-ended willingness-to-pay questionnaire (WTP).

German population pays national insurance contributions into the health system, so people are not used to pay additional contribution for health. Therefore they may eye suspiciously any kind or even possibility of co-payment. This might lead to a misunderstanding of WTP or may cause a great number of protest answers. First Results are shown to demonstrate the degree of acceptance about WTP questions for cost-benefit analyzes in German health system. Women’s preferences for the two models will be discussed.

Start and end date of study:
2/2007-1/2010
The study strictly adhered to “Good Clinical Practice”.

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The German multicenter trial midwife-led unit

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Background: In Germany, the majority of women (98%) give birth in a hospital. The birth process is strongly medically controlled. Less than 10% of all hospital births of low-risk women occur without any medical interventions. Results of international studies show that intervention rates in midwife-led units are lower than in obstetrician-managed units with a positive neonatal and maternal outcome. The first midwife-led unit in Germany was opened in 2003. Up to now seven units exist.

Methods: A prospective controlled multicenter trail comparing the two models of care in four hospitals with midwife-led units was conducted. Healthy pregnant women meeting the criteria for inclusion and agreeing to take part in the research choose either the midwife-led care or the standard obstetrician-managed care. Documentation was designed and is completed by the midwives during labor. The participants receive posted questionnaires eight weeks and six months after birth. The main outcome variables are maternal and neonatal morbidity, mode of delivery, medical interventions, postnatal physical symptoms, postnatal wellbeing and breastfeeding. Groups are compared using an intention-to-treat analysis.

Start and end date of study: February 2007 until January 2010. The study strictly adhered to “Good Clinical Practice”. Ethics approval was obtained. This study was supported by funding from the Federal Ministry of Education and Research in Germany.

Results: Results will be available in Summer 2009.

Conclusion: Up to now (31.03.2009) the sample contains of over 900 participants. The response rate of both questionnaires is at approximately 95%.

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Outcomes of a clinical trial comparing midwife-led care and obstetrician-managed care for low-risk women in Germany

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Background: In Germany, the majority of women give birth in a hospital. Less than 10% of all hospital births occur without any medical interventions. Results of international studies show that intervention rates in midwife-led units are lower than in obstetrician-managed units with a good neonatal and maternal outcome. The purpose of this prospective controlled trial was to examine the outcomes of low-risk women and their children in the midwife-led model of care compared to the obstetrician-managed delivery unit.

Method: A convenience sample of 238 women was obtained. Documentation was designed and completed during labor by the midwife. A self-reported questionnaire using established instruments and self-designed scales was designed. Women received the posted questionnaire eight weeks after birth.

The main outcome variables were maternal and neonatal morbidity, mode of delivery, medical interventions, postnatal physical symptoms, postnatal wellbeing and breastfeeding. Groups were compared using an intention-to-treat analysis.

Start and end date of study: February 2004 until January 2007. The study strictly adhered to “Good Clinical Practice”. Ethics approval was obtained. The study was supported by funding from the Federal Ministry of Education and Research in Germany.

Results: Results show a significantly lower rate of medical interventions, a significantly higher rate of normal vaginal deliveries and a significantly higher rate of exclusive breastfeeding experienced by women in the intervention group.

Conclusion: The midwife-led care offers real benefit for low-risk women and their children during labor and birth, with an increased likelihood of a normal birth.

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Uterine rupture on trial of labor in attempted vaginal delivery after C-section – case report

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Background: There is significant controversy about risks related to attempted vaginal birth after caesarean (VBAC). Studies indicate VBAC to be a safe option for women with a history of one previous caesarean section.

Case Report: 36 years old multiparous (parity 3) with previous caesarean (15 years before) and 2 VBAC prior to index pregnancy was admitted to our facilities with over 41 weeks pregnancy for a TOL. The pregnancy was uneventful. Maternal and fetal well being were assessed prior to TOL. Initial Bishop score of 2. TOL was performed with a vaginal slow releasing dinoprostone system. Vaginal bleeding and fetal bradychardia were diagnosed shortly after admission at the delivery room. An emergency caesarean was performed and a 3100g male infant was delivered with an Apgar score of 2 at the first minute and required respiratory aid. During the procedure hemoperitoneum and uterine rupture of the low segment/left anterolateral uterus wall was noted. Total Hysterectomy was performed. The infant was admitted to the neonatal intensive care unit and required respiratory assistance for less than 12 hours. Transfontanellar doppler ultrasound scan was performed at D2 and was reported as normal. At D7 both mother and a healthy infant were discharged. At 6 months follow up the infant showed normal growth and development.

Discussion: Uterine rupture remains one of the most frightening complications in obstetric care. Although many studies claim the relatively small risk of uterine rupture during vaginal birth after caesareans, the induction of labor may increase greatly this risk.

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Asymptomatic horn rudimentary pregnant uterine rupture with a viable fetus

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An asymptomatic ruptured rudimentary horn pregnancy in a 31 year old, second gravida is reported. She was referred to our maternity for anhidramnios at estimated gestational age of 30 weeks. An advanced abdominal pregnancy was diagnosed with sonographic features suggestive of horn rudimentary uterine rupture. Elective laparotomy was performed and a healthy infant was delivered. Excision of the rudimentary horn was done and an uneventful recovery followed. Authors suggest that an unusual sonographic appearance of the placenta with anhidramnios must first lead to consider the diagnosis of advanced abdominal pregnancy in time to save the surgeon from an unpleasant and dangerous surprise.

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Doppler flow ultrasound diagnosis of massive fetomaternal transfusion (FMH): a case report

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Massive fetomaternal haemorrhage (FMH) has an incidence of approximately 1:1.000 deliveries. In most cases, the cause is not identified. The clinical manifestations and the prognosis of a FMH depend on the volume of the haemorrhage and the rapidity with which it has occurred.

A 30-years-old primigravida was hospitalized at 38 gestational weeks because of constrict to silent fetal heart rate pattern with sporadic decelerations, oligohydramnios and decreased fetal movement. Her past gestational history was non-contributive, 0, Rh-negative blood type with regular anti-D-prophylaxis. We saw a normal fetal growth and no reference of retroplacental haematoma in the ultrasound examination. The Doppler flow examination presented normal indices in the fetal umbilical and middle cerebral artery, but strong increase of the Vmax (120cm/s) in the middle cerebral artery. A rapid caesarean section was performed by a suspicion of a fetal anaemia on the base of fetomaternal transfusion. The infant with Apgar score of 4, 7, 8 presented a severe anaemia (Hb 5g/dl) and received a rapid blood replacement. The Kleihauer-Betke test stain showed a massive fetomaternal transfusion. To prevent further Rh(D)-immunization of the mother we administered 9 doses of Rhophylac® 300 intravenously. Further postpartum course was normal.

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Spontaneous Uterine Rupture in a primigravidarum woman after laparoscopic cornual resection: a case report

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Uterine defects in pregnancy are a very rare obstetric complication. Defects involving the myometrium encompass entities such as uterine rupture, dehiscence, sacculation or diverticulum. It can cause severe problems for the mother and child if not immediately diagnosed and treated. This case report describes spontaneous uterine rupture in a healthy 30-year-old primigravid woman at the 31st gestational week. The woman was hospitalized due to acute abdominal pain. At that time, the fetal monitoring notified reactive fetal heart beat and no contraction. The diagnosis of uterine rupture esp. dehiscence, evoked in the presence of acute abdominal pain, unruptured fetal membrane out of myometrium like an hourglass on ultrasonography. An emergent caesarean section was performed and a rupture of right cornual uterine area found. Her physician had known that she had no known risk factors explaining the rupture. However, she had an operative history for ectopic pregnancy.

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Strict diagnosis of intrauterine infection during labor and the incidence of early onset neonatal sepsis

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Objective: Prospective evaluation of a protocol for diagnosis of intrauterine infection during labor (IUI).

Methods: For more than one year rectal temperature was measured 2-hourly in all women (n=3075) with gestational age ≥36 weeks and singleton pregnancy, admitted in active labor, until 2 hours after delivery. Intrauterine infection (IUI) was defined by a temperature ≥38.5 C or a temperature ≥38.0 C with 2 of the following signs of infection: (T. E. M. P) Tachycardia of the fetes ≥160, Elevated leucocytes ≥16.10^9/L, Meconium stained or offensive liquor, Pulse mother: maternal tachycardia ≥100. Women with IUI were treated with amoxicillin and gentamycin i. v. Women with a temperature ≥37.5, but without IUI, were classified as suspect and infants stayed for 24 hours observation. The remaining women were classified as normal. Endpoint of the study was neonatal infection within one week, classified as I. sepsis with positive blood or liquor culture, II. possible infection based on clinical signs, III. prophylactic antibiotics without clinical signs of infection.

Results: 90 women (2.9%) were diagnosed and treated as IUI, 364 (11.8%) were classified suspect. One infant (0.3/1000) had E coli sepsis, 2 infants GBS sepsis (0.7/1000), 31 infants (10/1000) had possible infection and 88 infants (29/1000) were treated prophylactically. The remaining infants (959/1000) had no signs of infection.

Conclusion: With the current strategy GBS sepsis rate was slightly higher than recently reported from USA with GBS screening at 35-37 weeks and prophylactic treatment, while carrier rate was similar (22%) and antibiotic prescription rate during labor was only 2.9%.

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Ventilator Delivered Mask Ventilation: Comparison of 3 standards methods of bag and mask ventilation with a new method ventilator provided mask ventilation for neonatal resuscitation

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Background: Neonatal resuscitation is common and lifesaving. Optimum resuscitation involves delivery to the newborn lungs of sufficient ventilation to provide gas exchange whilst minimizing risks of barotraumas and hypocarbia. Mannequins are commonly used to train various forms of bag and mask manual ventilation with little research on effectiveness. This study aimed to measure this variation in 3 standard modes of mask ventilation compared to ventilator delivered mask ventilation (VDMV).

Methods: Respiratory function monitor, a modified resuscitation mannequin and a computer where used to measure delivered airway pressures, tidal volumes, minute ventilation and inspiratory times to the mannequin “lungs” in model of neonatal resuscitation. Thirty six participants gave positive pressure mask ventilation targeting a rate of 60 breaths per minute, pressure of 18/5cm H2O with adequate chest excursion to a mannequin for three minutes with each of the four mask ventilation methods. Each mode was randomly sequenced with 3 minutes of rest between each mode.

Results: 21,136 inflations were recorded and analyzed. No significant differences were seen in peak inspiratory pressure between modes. VDMV had significantly lower variation in all other measured parameters (P<0.001). Laerdel bagging delivered tidal volumes and minute ventilation over twice that delivered by VDMV and Neopuff (p<0.001).

Conclusions: during a simulated 3 minute resuscitation of an apneic term baby on a mannequin VDMV produced the least variation in delivered ventilation. Anaesthetic bag and Laerdel self inflating bag produced wide variation and unacceptably high tidal volumes and minute ventilation.

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A case of HELLP Syndrome in primigravida carrying twins
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Introduction: HELLP Sy is a form of severe preeclampsia, found in 4-12% of pregnant women suffering from this clinical condition. The syndrome consists of the following triad: Haemolysis, Elevated liver enzymes and Low platelets. The HELLP syndrome can be found isolated or accompanied with all symptoms of the EPH complex.

Aim: The aim of this study is to present a case of appropriately and in due time diagnosed and treated HELLP syndrome in primigravida carrying twins.

Case study: A twenty-nine year old primigravida carrying twins was examined. She was in the 25th week of gestation and was admitted to hospital due to pain in the epigastrium and right subcostal area, accompanied with nausea and vomiting. The patients BP was 140/100mmHg, and the laboratory test Results proved anaemia (Hb=86g/L, RBC=3.13x1012/L, Hct=0.27); thrombocytopenia (PLT=80 000/mm³); elevated liver enzymes (ALT=144 IU/L, AST=215 IU/ L). The patient was transmitted to the Clinic for Gynecology and Obstetrics where the pregnancy was terminated. The decision was made upon the severe clinical condition and the fact that twin pregnancy in early week of gestation was in question.

Conclusion: Symptoms found in HELLP syndrome are non-specific, thus it can often be misdiagnosed with hepatitis, atrophia flava hepatis, purpura thrombocytopenica and syndroma haemorrhagicum. Therefore it is important to recognize the symptoms of the HELLP syndrome as soon as possible, and if needed to terminate the pregnancy in due time. All these measures help prevent hepatic coma development and patient’s exitus

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Antenatal invasive treatments in monochorionic gestations

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Monochorionic pregnancy occurs in 20-30% of multiple gestations. In 10-15% of these twin-to-twin transfusion syndrome may occur. Ultrasonography is of primordial importance for diagnosing chorionicity, major abnormalities, evaluation of chromosomopathies markers and for the therapy of this syndrome. The authors present two patients with twin-to-twin transfusion syndrome beginning on early second trimester (weeks 14 and 16). Both were treated by laser fethoscopy at King’s College Hospital. In both only the receptor fetus survived. We conclude that the outcome for the giving fetus is very reserved (antenatal mortality rate is higher - 18 to 35%). Laser therapy can improve mortality rate on the receptor fetus and potentially reduces neurologic morbidity.

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Congenital cystic adenomatoid malformation (CCAM) associated to fetal hydrops in a diamniotic-dichorionic pregnancy

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Introduction: CCAM represents 25% of congenital lung malformations, but 75% of those with prenatal diagnosis. CCAM Results from an abnormality of branching morphogenesis of the lung, due to a mistake in the maduration of bronchiolar structures. The survival rate is usually good (70-85%).

Case report: 21 years-old patient, without pathological antecedents. Blood group O Rh positive with negative serologies and indirect Coombs test. Diamniotic-dichorionic spontaneous pregnancy, with correct gestational controls.

At 23rd weeks of gestation a left thoracic hiperecogenic mass of 40x60mm that moved completely the heart was found in one of the fetuses, suggesting CCAM type III, associated to skin edema, pleural effusion, ascites and polyhydramnios. No abnormalities were found in the other fetus.

Postnatal confirmation of the diagnosis of CCAM was made, doing at 40 days of life, a left upper pulmonary lobectomy, with a good course afterwards.

Discussion: CCAM and shift of the mediastinum may lead to obstruction of the inferior vena cava and cardiac compression, Resulting in the development of hydrops from increased central venous pressure. Hydrops is associated with a minority of fetus with CCAM (8-10%), and usually occurs in big malformations.

The size of the lesion and the presence of hydrops are the determinant neonatal prognostic factors. The survival rate of non-hydropic fetuses is almost 100%, while with hydrops is less than 10%.

It is important to point out the infrequent association of CCAM and hydrops, and the good postnatal course of the newborn.

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Obstetrical and perinatal outcome in twin-to-twin transfusion syndrome

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Objective – Twin-to-twin transfusion syndrome (TTTS) is the Result of an intrauterine blood transfusion from one twin to another twin. TTTS represents a condition that develops in about 10-25% of monochorionic twin pregnancies. Our paper is targeting to evaluate the obstetrical and perinatal outcome in TTTS pregnancies.

Methods – our research has been developed on a lot of 29 patients diagnosed with twin pregnancies, between 1/2006 and 1/2009. There have been identified 7 twin pregnancies presenting TTTS (24.13%). The diagnostic pattern included: same sex of the fetuses, thin membranary septum, stuck twin aspect, lack of the lambda sign, Doppler anomalies, one hydramnios sack and one olygoamnios one, weight discordance, urinary bladder identification, nuchal translucency or small CRL.

Results – there have been diagnosed 6 monochorionic and 1 bichorionc twin pregnancies with TTTS. Pregnancy outcome for the 7 cases with TTTS consisted in 2 vaginal deliveries and 5 caesarian sections. Significant birth weight discordances occurred in all of the cases with TTTS. One case of severe TTTS in a bichorionic twin pregnancy with in utero fetal death and mummification of the dead fetuses. Placental vascular anastomoses were detected in 100% of the cases. In 6 cases with medium or low grade of TTTS, perinatal outcome was satisfactory.

Conclusions – TTTS is a serious fetal condition which can lead to unfavorable maternal and fetal prognosis when unidentified or untreated. Death of one fetus in TTTS can lead to neurological lesions or intravascular disseminated coagulation with a somber prognosis for the living fetus.

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Use of modified ultra-thin fetoscope for laser coagulation of placental anastomoses in twin-to-twin transfusion syndrome significantly improves neonatal outcome

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Objective: The laser coagulation of placental anastomoses is nowadays the standard treatment of twin-to-twin transfusion syndrome (TTTS). The main complication of fetoscopy is the iatrogenic induced preliminary rupture of the membranes (PROM), which significantly increases the rate of prematurity accompanied by worse neonatal outcome. The extent of the fetoscopical damage of the amniotic membrane could be responsible for PROM.

Materials and methods: The neonatal outcome after laser coagulation of placental anastomoses was compared in prospective study between groups with TTTS staging II to IV and 16th-26th weeks of gestation using modified ultra-thin sheath and flexible 1.0 to 1.2mm optic (n=15) and standard inflexible 2mm optic (n=45) (Karl Storz, Germany).

Results: The survival rate for at least one child was 100% in ultra-thin fetoscope group vs. 97.1% in inflexible fetoscope group and 90% vs. 74.3% for both. Using ultra-thin equipment significantly prolonged the duration of the pregnancy from 231.5±27.2 days to 252.8±15.7 days (p<0.05). The neonatal weight of donor twin was significantly increased in ultra-thin fetoscope group from 1753±725 to 2,424±840g (p=0.04) and 1963±691 to 2519±734 of recipient (p=0.06). The TTTS staging, GA, APGAR 5min and used laser energy were not significantly different between both groups.

Conclusion: The reduction of the extent of the fetoscopic amniotic membrane damage using modified ultra-thin fetoscope for laser coagulation of placental anastomoses in patients with TTTS significantly improves neonatal outcome.

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Air transfer of patients with twin-to-twin transfusion syndrome for laser coagulation of placental anastomoses does not deteriorate the neonatal outcome

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Objective: Laser coagulation of placental anastomoses has become the preferred treatment of twin-to-twin transfusion syndrome (TTTS), significantly improving the neonatal outcome. In spite of air travel becomes increasingly common, no epidemiological studies have been conducted so far to verify the effects of air flight on the neonatal outcome after laser coagulation for TTTS treatment.

Materials and methods: Prospective study was performed in 60 patients with TTTS staging II to IV between 16th and 26th weeks of gestation. 12 patients had been transferred by air >2h for laser treatment in our center. Amniodrainage was performed before air travel in 5 cases. Laser coagulation was performed using a 0.4mm Nd: YAG-laser 50 watts and Storz optic.

Results: TTTS staging and gestational age did not differ between air transferred patients and control group. APGAR 5min, fetal weight, duration of pregnancy (239±22 in air travel group vs. 232±27 days in control group), used laser energy and amniodrainage (1764±983 vs. 2432±1246ml) were not significantly different between both groups. Following laser coagulation, the survival rate for at least one child was 100% in air transferred patient group vs. 97.1% in control group and 80% vs. 79.4% for both.

Conclusion: Air transfer of patients with TTTS for laser coagulation of placental anastomoses does not deteriorate the neonatal outcome.

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Twin pregnancy achieved by IVF/ET: Evaluation of the course and outcome

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Introduction: Despite contemporary approach, multifetal pregnancies achieved by assisted reproductive technologies still remain the challenge in clinical practice. The aim of the study was to evaluate the link between duration of gestation, neonatal morphometric parameters and condition at birth, and the mode of delivery of twin pregnancies achieved by IVF/ET procedure.

Material and methodology: Throughout the 12-months-period we examined 37 patients with twin pregnancies achieved by IVF/ET, aged 25-48 year; 8 patients underwent natural delivery and 29 patients underwent Caesarean section (22 elective and 7 emergency).

Results: Indications for elective Caesarean deliveries were older age and malpresentation; neonatal Apgar score was 7-9, and neonatal birth weight 2,100-3,150g. Indications for emergency Caesarean sections were: coming fetal asphyxia, malpresentation and premature rupture of membranes; this group had lower gestational age at delivery, neonatal Apgar score was 3-6, and neonatal birth weight 1,000-1,750g. Naturally delivered patients were younger than 31 years, gestational age at delivery was above 37 gestational weeks, first twin mostly had occipital presentation, Apgar Score was high, and neonatal birth weight was higher (2,700-3,150g). All the children had adequate postnatal adaptation.

Conclusion: Course and outcome of twin pregnancies achieved by IVF/ET does not differ from spontaneously achieved twin pregnancies. Additional risk factors are older patients age and malpresentation. Apgar score is lower at emergency Caesarean delivery-born-babies, especially if their gestational age was lower. Vaginally-delivered patients had the best outcome due to the higher gestational age at delivery. Puerperal course at all the patients was as usual.

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Monochygotic, monochorial triplets

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Incidence of monochorial, monoamniotic triplets pregnancy is rare (1:10 Mio. – 1:200 Mio.). Already monochorial twins show placental anastomoses in nearly all cases (fetofetal transfusion syndrome 10–20%). The risk of fetofetal transfusion syndrome in monochorial triplets is even higher. Therefore the possibility of a fetal reduction (fetocid with cord ligation or cord coagulation) or even in rare cases an abruption should be discussed. Case report: A 38-year-old woman (GII/PI, caesarean section in anamnessis) with monochorial triamnial triplets in 21+5 weeks of gestation presents for consultation (spontaneous conception of pregnancy, no assisted reproduction, no ovarian stimulation). Secondary finding is a low insertion of placenta with a chorangiomi of 7cm. All fetuses are normal developed no signs of fetofetal transfusion can be detected in ultrasound. Pregnancy is uncomplicated for mother and fetuses. They develop concordant without signs of fetofetal transfusion (weekly doppler-sonography). Caesarean section in 32+5 weeks of gestation follows (weight I: 1490g, weight II: 1610g, weight III: 1760g, no anemia). Radiological and a histological examination of the placenta is carried out. Conclusion: Spontaneous monochorial triplets are rare. Maternal and fetal risk is very high, therefore decisions of fetal reduction or interruption are made. In this case we describe an uncomplicated pregnancy for mother and fetuses. With frequently consultation of Gynecologist pregnancy is prolonged until 33 weeks of gestation with good maternal and fetal outcome.

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Managing the triplet pregnancies

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Objective: To present the course and outcome of 85 triplets during the 15-years period trying to find out if antenatal preventive strategies and interventions during the early neonatal period affect perinatal outcome.

Methods: I Standard care (N=44) bed rest with routine hospitalization after 28–32 weeks, routine clinical and ultrasound examinations, biophysical profile and non-stress tests from 28 weeks, no free access to surfactant or parenteral nutrition.

II Modified care (N=41) bed rest with routine hospitalization after 32 weeks, biophysical profile, non-stress tests and doppler analysis from 26 weeks, free access to surfactant and parenteral nutrition.

Results: The incidence of caesarean sections was significantly increased in group II (P=0.014). Infants in group II had less frequently uneventful early neonatal period, mainly due to significantly increased conatal infection (P=0.007) and neonatal encephalopathy (P=0.001). Perinatal mortality was decreased from 235% (group I) to 142% (group II) for newborns reached 24 weeks or more. None of children <1,000g died in utero in group II. Early neonatal death of infants >1,500g was significantly reduced in group II (P=0.048).

Conclusion: Advances in neonatal care and infants in better overall condition improved outcome of triplets managed by modified care. A higher caesarean section rate because of imminent fetal jeopardy could be the explanation for lowered perinatal mortality and significantly improved outcome in very preterm infants from triplet gestations

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Amniocentesis without risk: A dream or reality? Evidence based introduction of atraumatic 29 gauge needle

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Objective: Amniocentesis (AC) is the gold standard for invasive prenatal diagnosis. The risk of procedure for fetal loss is 0.25 to 1%. The main complication of AC, especially in case of chorio-amniotic dissociation, is the leak of amniotic fluid complicated by amnion infection and abortion.

Materials and Methods:
(A) Prospective study using 29 gauge (G) needle (HVM Filtramed, Rothenburg/Fulda, Germany) for AC in 58 patients with 16 weeks of gestation with chorio-amniotic dissociation.
(B) In-vitro comparison of the damage area of human amniotic membrane and amniotic fluid loss between 22G (diameter 0.7mm) and 29G (0.34mm) needles (n=9).

Results
(A) The AC could be performed in all patients. The mean amount of obtained amniotic fluid was 12.6±1.3ml. We did not have any complications or fetal loss after AC.
(B) The mean hole area after using 29G needle was 25055±1897 µm² compared to 158746±181808 µm² of 22G needle (p=0.00065). The mean amount of amniotic fluid loss in 5 min was 0.008±0.031ml/5min using 29G needle and 26.27±14.61ml/5min, respectively (p=0.000001). Microscopic investigation of damaged areas of amniotic membranes using 29G needles at the end of experiments showed that the small holes were plugged by particles and cells of amniotic fluid. The holes after using 22G needles remained open.

Conclusion: We claim that the use of atraumatic 29G needle must reduce the risk of amniocentesis to nearly zero due to complete plugging the damaged hole of amniotic membrane by particles and cells of amniotic fluid.

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Success Prognosis of immunoglobulin injection into fetal abdominal cavity for pregnancy with blood type incompatibility (anti-M antibody): A case report

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Background: Irregular antibodies are usually detected in 0.3% of all pregnancies. We present here a case of severe fetal anemia caused by anti-M antibody positive for pregnancy with blood type incompatibility, which showed a favorable course only with immunoglobulin therapy into fetal abdominal cavity (IFAC).

Case: The mother was 23 years old (gravida 0 and para 0), and had no history of transfusion. Anti-M antibody was detected in the maternal cross match test at the 16th gestational week, and the antibody titer was 1:1024 in the indirect Coombs’ test. Fetal middle cerebral artery peak systolic velocity was elevated to 77.8cm/s at the 30th gestational week. The umbilical blood hemoglobin (Hb) level was 6.4g/dl and the Result of the direct Coombs’ test was positive. IFAC was performed 4 times at a dose of 2g/kg estimated body weight. The Hb level improved to 11.5g/dl without fetal transfusion. The mother delivered a female baby weighing 2,605g at 38 weeks. The Hb level at birth was 15.4g/dl and exchange transfusion was not required.

Conclusion: In general, fetal transfusion is required for the treatment of fetal anemia in pregnancy with blood type incompatibility. In the present case, IFAC was induced an excellent response. Since there are few reports on such administration of immunoglobulin, accumulation of more cases is required to prove its efficacy. Nevertheless, this procedure is promising as one of the treatment options for pregnancy with blood type incompatibility considering the merit of a heat-treated product.

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The evaluation of the course of hemolytic disease in the intrauterinely treated newborns with fetomaternal incompatibility – the own experiences

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Introduction: Fetomaternal incompatibility can result in hemolytic disease of the fetus and affect the newborn health.
Aim: The analysis of selected clinical and biochemical parameters in the newborns with fetomaternal incompatibility who were given intrauterine fetal transfusions.
Methodology and material
24 disease histories of the newborns born from 01.01.2004 to 31.12.2008 in the Obstetrics and Gynecology Clinic I of the Medical University of Warsaw were analyzed retrospectively. They were given intrauterine transfusions. The newborns were at the fetal age of 34-37 weeks. On average, 1-9 transfusions were given to one fetus due to hemolytic disease connected with the presence of antibodies in Rh (anti-D) and in the Duffy, Kidd and Kell system.
Results: Hydrops fetalis was diagnosed in 2 newborns (8%). Severe hemolytic jaundice with umbilical cord blood bilirubin levels over 5mg% was detected in 11 newborns (46%). Severe hemolytic anemia with the hemoglobin level below 10g/L was observed in 2 newborns (8%). One exchange transfusion was given to 11 newborns (46%), two transfusions to 4 neonates (16%), and in 3 cases (12%) three or more transfusions were necessary. Exchange transfusions were not needed in 6 cases (25%), and 20 newborns (83%) did not require supplementary transfusions.
Conclusions: Intrauterine fetal transfusions are an effective method of treating hemolytic disease. It decreases the incidence of hydrops fetalis and severe hemolytic anemia, reduces the number of exchange and supplementary transfusions in newborns.

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The use of erythropoietin to treat the late anemia in the isoimmune hemolytic disease of the newborn

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Background: Children with isoimmune hemolytic anemia can have an exacerbated physiological anemia at 12 weeks, required blood transfusions, because of the transplacental passage of IgG antibodies and specific anti Rh- antibodies.

Material and method: We studied the evolution of a number of 90 newborn children with hemolytic isoimmune disease, hospitalized between 2006 – 2008.

Results: A number of 90 newborn children (1.33%) had the isoimmune hemolytic disease; 10 patients (0.14%) had Rh immunization and 80 (1.19%) ABO immunization. The severe forms of hemolytic disease through Rh immunization needed exchange transfusion, the other newborns being treated with packed red blood cells transfusions and /or phototherapy. From children with ABO immunization, 3 cases needed exchange transfusion (all presenting anti-A antibodies), 49 cases developed medium severity forms of the disease and 28 mild forms.

For 9 children (2 with Rh immunization, 7 with ABO immunization) were prescribed erythropoietin (Neorecormon) at the age of 2 weeks in doses of 250 UI/kg, 3 doses/week, for 4-6 weeks for the prophylaxis of late hemolytic anemia. None of the patients needed blood transfusions.

Conclusions: The use of erythropoietin in stimulating the erythropoiesis after an isoimmune hemolytic disease, studied from the perspective of the cost/benefits rapport is a therapeutical alternative.

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New reference ranges for middle cerebral artery peak systolic velocity (MCA-PSV) and their applicability in diagnosing fetal anemia in pregnancies at risk

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Objectives were to assess accuracy of MCA-PSV in normal and complicated pregnancies, evaluate impact of gate-placement and angle-correction, establish reference ranges and assess their applicability in diagnosing fetal anemia.

In 166 low-risk pregnancies MCA-PSV was measured at 2 locations with and without angle-correction. Reference ranges were established with linear regression. We compared them with existing ranges. In 34 fetuses at risk for anemia MCA-PSV was measured and plotted over our curves. If values suggested anemia, FBS or laborinduction was performed. MCA-PSV was expressed in Z-scores, Hb in MoM. Correlation was evaluated by linear regression. We calculated accuracy data for MCA-PSV>1.645 Z-score in predicting Hb<0.65MoM.

In the low-risk group (N=126) the best regression between gestational age (GA) and MCA-PSV was linear (mean=-16.99+2.10GA, 95th-centile=mean+1.645SD). Intraobserver (0.96-0.98) and interobserver agreement (0.99) were high. 15/34 fetuses at risk for anemia did not need IUT. 6 FBS were performed because of anomalies. 1 fetus was anemic, 10 fetuses born alive were non-anemic. Of the other 19, 14 had IUT, 5 had laborinduction. 16/19 were anemic. Correlation was negative (r=-0.69, p<0.0001), sensitivity 91%; specificity 91%; PPV 83% and FPR 6%.

In conclusion, our reference ranges can be applied to complicated pregnancies. Due to a persistent negative correlation between MCA-PSV and fet. Hb these ranges could be used for all types of anemia. The high sensitivity and PPV indicate that a high MCA-PSV is a strong indicator of fetal anemia. The high intra- and interobserver agreement reflects high reproducibility and argues for MCA-PSV to be goldstandard in diagnosing fetal anemia.

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Rhesus alloimmunization – pregnancy outcome in a tertiary care hospital in Portugal

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Rhesus (Rh) alloimmunization, once considered a major cause of perinatal morbidity and mortality, is becoming a rare event since the general administration of rhesus immune globulin. However, this prophylactic measure is not always performed, and when the Rh autoantibodies cross the placental barrier, the fetus can suffer variable degrees of hemolysis, which may lead to fetal anemia, hydropsis and ultimately death. Neonatal jaundice is a common finding in the alloimmunized newborn, which can lead to kernicterus.

The purpose of this retrospective study is to evaluate the fetal and neonatal outcome of pregnancies with Rh alloimmunization diagnosed from January 2002 to December 2008 in Hospital de Santa Maria, a tertiary care hospital in Lisbon, Portugal.

During this time period 13 cases were referred. Mean maternal age was 33.6 years, ranging from 26 to 43; all women were multiparous. In one case, Coombs test titles remained stable, and no other diagnostic procedure was performed. The remaining cases needed additional diagnostic procedures, namely peak MCA Doppler velocity (12 cases) and amniocentesis for \( \Delta OD_{450} \) (2 cases). In two cases moderate to severe fetal anemia was detected, and intrauterine transfusion was needed. No perinatal deaths occurred. Seven babies were delivered at term, and the remaining 6 were born preterm (>32 weeks). Neonatal outcomes (birth weight, Apgar scores, neonatal hemoglobin, hyperbilirubinemia, days until discharge, need for blood transfusion or exchange transfusion) were evaluated.

Despite the seriousness of this condition, favorable outcomes can be expected if these pregnancies are carefully surveilled in a tertiary center.

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Association between serum magnesium level and Impaired glucose tolerance test in pregnancy

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Abstract:
Introduction & objective: Magnesium deficiency in non pregnant women increased oxidative stress and Supplementation of Mg recovered Insulin sensitivity and in pregnancy Mg also induced harmful effect on Glucose manage. Some elemental contents in serum of pregnant women were changed such as Cu & Zn, they decreased with gestational age but Ca increased. Level of Mg Serum in diabetic pregnant women decreased.

Material & methods: In descriptive prospective study we have 440 pregnant women That coming for prenatal care and we screened Gestations Diabetes mellitus and checked level of serum Mg.

Results: The average of gestational age was 25±3.2 (20-28). Average of parity and age of mother was 1.3±0.7 (1-8),28.2 (17-42) respectively, Impaired GCT was %19.5 (GCT >130) Impaired GTT was 4%. Serum Mg level was normal (1.8-29mg).

Conclusion: There is no association between serum Mg level and impaired Glucose Tolerance test.

Key words: Serum Mg, GCT, GTT.

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Relationship between hyperemesis gravidarum and Helicobacter Pylori

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Severe nausea and vomiting associated with weight loss, ketonemia, and electrolyte imbalance in pregnancy is called hyperemesis gravidarum (HG). Its cause is unknown but there are some hypotheses like hormonal mechanisms, psychological and emotional factors and Helicobacter Pylori infection. The aim of this study was to find an association between (HG) and H. Pylori infection. For this purpose in a prospective study from Aug. 2001 to Feb. 2002, the serum antibodies against H. pylori in 39 patients with HG were compared with IgG titers of 55 asymptomatic pregnant women at the same gestational age as controls. Venous blood was taken after the patient had given their written consent. Specific serum antibodies (immunoglobulin IgG) directed against H.pylori was measured by fluorescent enzyme-immunoassay. IgG titers less than 15 was considered negative, IgG titers more than 20 were regarded positive and IgG titers between 15-20 were considered as suspicious and required repeating the test after 2-4 weeks. Chi square, Mann Whitney and Student t test were used for statistical analysis of the data. positive serum IgG concentration were found in 26 of the 39 hyperemesis patient (66.7%) compared with 23 of 55 controls (41.8%). The difference was statistically significant (p<0.015). The mean IgG titers in hyperemesis group 25 compared to 10.5 in control group (p<0.05). It seems that H.pylori infection is significantly associated with HG.

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Prediction of severe infection – usefulness of chemokines in the umbilical cord blood of newborns

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Background: Early prediction and diagnosis of sepsis in preterm and term infants are one of the most serious problems in modern neonatology. Quick diagnosis is not easy because the symptoms of infection are often unspecific and subtle and may be similar to various non-infection conditions. In recent years, cytokines, including chemokines, have been purposed as markers for diagnosis of infection in adults, children and infants.

Method: We measured a panel of chemokines in the umbilical cord blood of newborns, who developed early sepsis, before their clinical presentation. The chemokine measured were MIP-1α, MIP-1β, RANTES, ENA-78 and GRO-α.

Results: Of 116 preterm and term newborns from prenatal infection risk factors, 18 were culture confirmed sepsis, 28 were culture-negative clinical infection, 22 involved non-infected episodes and 48 were healthy without any symptoms of illness. All studies chemokines except RANTES, showed up-regulation in newborns who developed clinical infection. RANTES showed significant down regulation in all infected preterm babies, but its values were without clinical usefulness in diagnosis of sepsis. Similar MIP-1α, MIP-1β and ENA-78 showed up-regulation in culture positive infected preterm or term newborns but without clinical worth. Only cord blood GRO-α >169.7pg/ml had sensitivity, specificity and positive predictive and negative values of 100%, 86%, 62% and 100%, respectively for identifying preterm patients who developed culture confirmed sepsis.

Conclusion: The chemokines helpful in diagnosing sepsis in adults, there were not usefulness in neonatology. Only GRO-α with other mediators of infection might allow predict and early detect preterm infants with sepsis.

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Early diagnosis of neonatal sepsis using an interleukin-6 rapid test combined with C-reactive protein in newborns with clinical suspicion of infection

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Aim: To evaluate the usefulness of interleukin-6 (IL-6) to predict the likelihood of neonatal sepsis in order to design an algorithm to decide antibiotic therapy.

Methods: IL-6 and C-reactive protein (CRP) were determined in 42 newborns with clinical suspicion of infection. Newborns were classified as a confirmed, probable or no infection, based on the Results of cultures, chest x-rays and the involvement of four or more clinical areas on a scale of eight. Samples for IL-6 were collected and frozen until its determination at the end of the study. Blinded IL-6 measurements were performed using a rapid test. Receiver operator characteristics curves (ROC) for CRP and IL-6 versus infection (confirmed or probable) were determined.

Results: 11 among 42 cases (26.2%) included in the study were classified as confirmed or probable infection. The area under curve (AUC) for IL-6 was 0.9, with a cut-off value of 53 pg/ml: sensitivity 90.91%, specificity 80%, positive predictive value (PPV) 62.5% and negative (NPV) 96% The level of IL-6>96 pg/ml and/or the combination of IL-6>53+CRP>13.3, were the markers that best predicted infection: specificity 100% and PPV: 100%.

Conclusions: Assessment of IL-6 could allow withholding or early discontinuing antibiotics in cases of IL-6<54 pg/ml. In newborns with IL-6>96 pg/ml and/or IL-6>53+ CRP>13.3, antibiotics should be started promptly, given the high likelihood of infection. Implementation of an algorithm based on the determination of IL-6 and CRP, in the initial assessment of newborns with clinical suspicion of infection, could reduce unnecessary antibiotic therapy.

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Usefulness of cord-blood serum C-reactive protein level and leucocytes from term and near-term newborns in a well baby nursery for sepsis screening: A pilot study

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Objective: Evaluate the usefulness of cord-blood (0h) septic screening from term/near-term babies admitted to a well-baby nursery.

Methods: All infants admitted during 1 year with risk of early sepsis. Observational study, all decisions taken by clinical team. Data collected from analysis (CRP/blood cell count) until treatment decision, peripheral blood-culture and clinical findings. A positive septic screening (indicating treatment) Results from a score involving CRP, leucocytes/neutrophil count. Newborns posteriorly classified as "probably infected/not infected" by the authors. Treatment decision at 0h, error of the negative predictive value and sensitivity where determined compared with 24h or posterior values.

Results: Newborns: 195 (35 with 0h values), 50.3% male, 37.9% born by caesarean section. Mean gestational age 38.7 (SD1.36) weeks. Mean birth weight 3,151g (SD459.65g). Risk factors: colonization with group B Streptococcus 33%, prolonged rupture of membranes 46.7%, maternal fever 16.9%, amnionitis 3.1%, maternal recent UTI without treatment 8.2%; multiple risk factors 8.2%. Screening at 0h determined just 1 treatment decision. Error of the negative predictive value 12% (4/33) and sensitivity 20% (1/5). Another 36 children (without 0h analysis) where treated for positive screening later (17 probably infected). All had good outcome.

Conclusion: The Results point to no need for cord-blood routine septic screening in well term and near-term newborns. Sensitivity is low and does not shorten significantly the hospital stay. Its omission does not carry worse outcome and reduces health costs. It should be reserved for selected high-risk situations. To be confirmed with a longer prospective study.

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Comparison effect of vitamin C vaginal tablet with metronidazole vaginal gel treatment and Relapse of bacterial vaginosis

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Introduction: Bacterial vaginosis is the common cause of abnormal vaginal discharge among women of reproductive ages.
Objective: This is a randomized clinical trial study to compare the effect of vitamin C vaginal tablet with metronidazol gel in treatment of symptomatic bacterial Vaginosis.
Methods: After confirmed diagnosis of bacterial vaginosis to Amsel criteria (at least 3 out of the 4 characteristic symptoms discharge, fishy odor, vaginal pH≥4.5, and presence>20% of clue cell), 60 non pregnant women of 15-45 years of reproductive ages enrolled in randomized clinical study, The women were randomly assigned to receive either 250mg vaginal tablet vitamin C once daily for 6 days (n=30) or vaginal gel.75%metronidazol 5gr once daily for 5 days (n=30). The two groups resulted comparable for demographics, history and baseline clinical picture. Participants were evaluated in two follow-up visits (after treatment and two week after treatment). Therapeutic success was defined as the presence of less than three of Amsels criteria.
Results: At the first follow-up visit, 23(76.7%) of women in vitamin C group and 24(80%) in metro gel group were cured. (P=0.7) at second follow-up visit two women (9.5%) in vitamin C group and one (5%) in metro gel group bacterial vaginosis was relapse.(P=999). Three women in vitamin C group and four in metro gel group were reported occasional burring and itching during product use.
Conclusion: Vitamin C vaginal tablet 250mg has effectiveness as metronidazol vaginal gel for treatment of bacterial vaginosis.
Key word: Bacterial vaginosis, Vitamin C, Metronidazole

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The influence of indomethacin on fetal cytokine production stimulated by bacterial LPS

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Subclinical infection plays an important part in preterm labor by initiating an inflammatory response of the mother as well as of the fetus. The fetal inflammatory response namely cytokine production seems to be involved in the development of white matter lesions in preterm babies. Recent studies suggest a protective role of indomethacin medication after birth. This study aims at exploring the in-vitro effect of indomethacin often given to mothers as a tocolytic agent in case of preterm labor on fetal cytokine production.

Methods: Cord blood mononuclear cells were incubated with LPS of E. coli- which in former studies had proven as a highly potent stimulator of cytokine production- and various concentrations of indomethacin with and without betamethasone. The levels of the proinflammatory cytokines IL-1β, IL-4, IL-5, IL-6, IL-8, IL-12, TNFα, INFγ, the chemokines MIP-1α and MIP-1β and the antiinflammatory cytokines IL-10 and TGFβ were measured by Elisa.

Results: Betamethasone diminished the production of all cytokines which could be stimulated by LPS. Indomethacin significantly stimulated the production of IL-10, even in combination with betamethasone. The secretion of IL-1β, IL-6, IL-8, IL-12, INFγ and MIP -1α was not affected by Indomethacin. TGFβ, IL-4, IL-5 and IL-15 could not be stimulated by LPS.

Conclusion: Indomethacin is not only a potent tocolytic agent, it may also stimulate the production of anti-inflammatory IL-10 which could prevent the fetus from the deleterious effect of TNFα on fetal white matter.

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The prevention of congenital fetal heart block in pregnant women with present anti SS-A and anti SS-B antibodies

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Anti-ribonuclein antibodies, present in Sjögren’s syndrome and SLE, may cross placenta and cause congenital heart block. It is still unknown why those antibodies cause problems in some pregnancies, while other pregnancies are uneventful.

The aim of this study is to present the pregnancy outcome in women with anti-ribonuclein antibodies and protocol used for the prevention of congenital heart block.

Methodology We treated 16 pregnancies in 3 women with Sjögren’s syndrome and 9 women with SLE and present anti-ribonuclein antibodies. If a) congenital heart block wasn’t present and/or there was no previous history affected fetus or if b) heart block was already present, we used Pronison in the treatment. If heart block hadn’t been present and women had previous child with congenital heart block we applied Dexamethason. We registered: gestational age at registration; fetal wellbeing; therapy applied and delivery data.

Results: Gestational age at first visit was 8 to 26 weeks gestation. There were 4 pregnancies with congenital heart block at registration; in 3 Resulting in stillbirth at 19 to 23 wg, and in one delivery at 32wg of affected neonate who died at 4th day inspite pacemaker. We successfully treated 5 patients with Dexamethason and 7 with Pronison therapy.

Conclusion: The treatment approach in pregnancies with anti-ribonuclear antibodies depends upon previous history. In the cases of no previous history of fetal heart block, regular treatment with pronison is recommended, but in the cases with previous history of fetal heart block long term therapy with Dexamethason is indicated.

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**Conservative treatment of patent ductus arteriosus in preterm neonates versus the use of cytooxygenase (COX) inhibitors**

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Introduction: The aim of the present study was to identify the effectiveness of conservative treatment versus the use of indomethacin for PDA closure, based on clinical assessment.

Method: One hundred and nine preterms were evaluated for PDA using clinical diagnostic criteria. None received prophylactic indomethacin. Patent ductus arteriosus was diagnosed in 17 neonates, using clinical signs. Group A received conservative treatment (oxygen, diuretics), while Group B received indomethacin. Each group was subdivided according to birth weight into two subgroups (≤1,000g) and (1,001-1,500g).

Results: Closure of patent ductus was observed in all of 6 patients who were born ≤1,000g and received only conservative treatment, while 66.7% (4 out of 6 born ≤1,000g) had their ductus closed successfully using indomethacin. 2 neonates born ≤1,000g and treated with indomethacin needed surgical closure.

Preterm with PDA, those who received CT (conservative therapy) and those who received COX (indomethacin).

Table 1

All those born 1,001-1,500g had their patent ductus arteriosus closed successfully using only conservative treatment.

Conclusion:

Birth weight plays a crucial role in the occurrence of persistent patent ductus arteriosus. It is clear that conservative treatment of PDA is effective, and probably should be considered more frequent, thus avoiding side effect of medications such and indomethacin.

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Fetal supraventricular Tachyarrythmia – permanent success with intermediate digoxin therapy

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Introduction: Fetal suprventricular tachyarrythmia is a severe fetal complication which appears between 20th and 30th week's gestation and may Result – if not identified - in fetal hydrops or even in stillbirth. Case: 40-years-old II Grav. Nullipara 19 weeks of gestation admitted with an acute episode of rheumatic arthritis. Ultrasound shows a normal developed male fetus with a supraventricular tachyarrythmia (230 bpm) associated with a pericardial effusion and ascites. Immediately a therapy with digoxin (Lanicor) was started until a digoxin blood level between 1.7 to 2.0ng/ml. The heart rate soon got back to normal, the fetal hydrops was unverifiable after some days. Afterwards an ambulant treatment with regular appointments twice a week in our outpatients clinic was possible until 30th week's gestation. Then the medication was tapered. The fetal heart rate stayed normal until 38+1st week's gestation. Due to fetal makrosomia and patient’s wish a primary caesarean section was performed. The newborn developed postpartal intermediate paroxysmale tachycardic episodes without the need of medication.

Conclusion: In literature only a few cases are reported where maternal digitalization was tapered without restarting of medication was necessary. Often these newborns need postpartal antiarrythmic therapy which was not necessary in our case. Tapering of digitalization already through pregnancy should be considered in some cases but with close fetal monitoring settings.

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Detection of the fetal high-grade atrioventricular block secondary to serious long QT syndrome using pulsed-Doppler echocardiography – a case report

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Case: We report a case of fetal long QT syndrome (LQTS) combined with 2:1 atrioventricular block (AVB), high-grade AVB and ventricular tachycardia (VT). At 35+0 weeks’ gestation, pulsed-Doppler echocardiography showed 2:1 AVB. It was replaced by high-grade AVB at 36+0 weeks and was associated with mild cardiomegaly. In high-grade AVB, the blood flow velocity waveforms of ascending aorta showed different shapes with variable peak systolic velocities and peak-to-peak intervals. At 36+5 weeks, VT appeared with moderate cardiomegaly and weighing 2,344 grams, male neonate was delivered by emergent Caesarean section. Electrocardiogram (ECG) at birth showed polymorphic VT and dissipation of VT was performed by intravenous administration of xylocaine and amiodarone. Following ECG revealed high-grade AVB with polymorphic premature ventricular contractions (PVCs) and markedly prolonged QT time of 920 msec. Based on these finding, LQTS was diagnosed and a temporary pacing was implanted immediately, however, ventricular refractoriness was so sustained that pacing was failed. Repeated episodes of Torsade de Pointes appeared and he died at 1 day old of age. LQTS3 was confirmed by genetic analysis of his blood sampling.

Discussion: Prenatal detection of high-grade AVB with the different shapes of blood flow velocity waveforms of ascending aorta with various peak systolic velocities and peak-to-peak intervals should be suspected serious LQTS with polymorphic PVCs. Pulsed-Doppler mode can be a useful diagnostic technique for AVB with polymorphic PVCs which is suggestive of serious LQTS.

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Biochemical markers of neonatal myocardial dysfunction

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Introduction: Little is known of biochemical markers of myocardial dysfunction in the neonate. Cardiac ultrasounds (US) are not always available at the bedside. Cardiac Troponin I (cTnI), CK-MB and NT-proBNP may be an alternative or complementary to influence evaluation and treatment.

Objectives: 1) To determine reference ranges of biochemical markers; 2) Their correlation to ultrasound findings.

Methodology: Cord and blood samples were collected from Full Term (FT) Appropriate for Gestational Age (AGA) infants of healthy mothers with uneventful pregnancies, upon parental consent, if clinically indicated. NT-proBNP was determined by VIDAS NT-proBNP, CK-MB and cTnI by chemoluminescence techniques.

Results: Median values for CK-MB declines from 79.0 to 43.0 U/L by the third day of live; cTnI rises from 0.004 to 0.066ng/mL by 72 hours falling to 0.0355 by 10 days; NT-proBNP peaks between 24 and 48 hours (3,303.0pg/mL), subsequently falling to 1179.5 pg/mL. Between 24 to 48 hours NT-proBNP significantly rose (p=0.045) with left to right shunt as per US changes.

Discussion: CK-MB, mostly of skeletal muscle origin in neonates, declines from birth reflecting delivery stress rather than myocardial injury per se further demonstrated by the higher values after vacuum extraction. The rise in cTnI may be explained by a degree of myocardial involvement, albeit physiological, or due to impaired plasmatic clearance. The initial rise and subsequent fall of NT-proBNP quite likely represents the physiological ventricular overload of transient birth adaptation, particularly with left to right shunt, physiological or pathological.

We are now studying other intrauterine or postnatal events.

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The psychological status and anxiety levels of pregnant women who undergo amniocentesis and chorion villus sampling (CVS)

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Purpose: This study has been made for descriptive purposes for the determination of problems suffered by and anxiety levels of pregnant women who have applied for amniocentesis and chorion villus sampling (CVS).

Method: The study has been conducted at the Prenatal Diagnosis Unit, in Ankara, Turkey. Sample group consisted of 241 pregnant women. The data collection form and Spielger's State-Trait Anxiety Inventory (STAI) have been used in the study. Percentage, Difference between Two Averages, Mann-Whitney U Test, One-Way Analysis of Variance, Chi Square, Kruskall Wallis One-Way Analysis of Variance tests have been used for statistical evaluation of the collected data.

Results: The most important reasons for subjecting pregnant women included within this study to amniocentesis/CVS have been established as high triple test Results (34.3%), advanced maternal age (30.9%), probability of chromosome anomaly of the newborn (19.7%), and having a child with anomalies in the past (15.9%). Throughout the amniocentesis/CVS process, 57.7% of pregnant women reported that they experienced anxieties about the operation, while 85.1% reported anxiety about the baby and 43.2% reported anxiety about their own health. The women's average anxiety score point averages who are applied amniocentesis/CVS process has been determined as 45.94 as anxiety in the middle levels. Average scores of state-trait anxiety of studied pregnant women have been found higher compared to their average scores in continuous anxiety (p<0.05).

Conclusions: We have recommended with regards interventions to reduce the problems and anxieties suffered by spouses applying to prenatal diagnosis units and to decrease their average anxiety scores.

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**Chorioamniotic membrane separation (CAS) after serial amniocentesis in polyhydramnion**

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In the first trimester amnion and chorion are separated, but after 16 weeks of gestation the chorionic cavity is obliterated by the amniotic cavity. Detachment of membranes may occur after amniocentesis when amniotic fluid dissects the space between chorion and amnion. Subsequent amniocentesis can be aggravated or impossible by this complication. The distance between amnion and chorion and the extent of separation so it can be divided into 1 minimal <3cm of the membrane surface, 2 small ><3cm but <25%, 3 moderate: 25-50%, 4 severe >50% but not complete and 5 CAS. We present a rare case of CAS occurred after 3rd amniocentesis for symptomatic polyhydramnion of unknown reason in a 28 years old III gravida/II para. TORCH serology was negative. Chromosomal analysis showed a normal karyotype. In 24 weeks amniocentesis and drainage (3l) was performed with a 18G-needle, followed by a second drainage (3l) in 27 gestational weeks and third drainage 29+0 (5l). In 31 weeks she had severe symptoms of polyhydramnion. Abdominal ultrasound showed a complete CAS. Patient was admitted and closely monitored. A 4th amniocentesis (3l) was performed. Umbilical cord flow was within normal ranges and the fetal biophysical profile was normal. In otherwise unremarkable pregnancies, clinician awareness of the possibility of amniotic band formation that might wrap around and constrict the umbilical cord following rupture of the amnion should be heightened. In patients with complete CAS serial ultrasound evaluation and close fetal monitoring are indicated. Knowledge of this potential life-threatening complication may identify cases in which cord compromise requires emergent delivery.

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Normal pregnancy outcome after repeated amnioinfusions from the 16th Week of gestation


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Purpose: To investigate the outcome of pregnancies with oligohydramnios or anyhydramnios due to amniocentesis, after repeated amnioinfusions from the 16th week of gestation.

Materials and Method: We studied 4 pregnant women who had amniocentesis for genetic reasons during the 16th week of gestation and were found to have premature rupture of membranes in the following 48 hours. After informed consent, they were submitted to repeated infusions of normal saline inside the amniotic cavity, every 4 weeks, while they were under close clinical, laboratory, and ultrasound follow up. The potential development of pulmonary hypoplasia, skeletal dysplasias, fetal distress, chorioamnionitis, sepsis, preterm labor, placenta abruptio, and neonatal-maternal mortality were investigated.

Results: None of the above-mentioned complications was found in any of the 4 pregnancies which were under examination. The neonates were almost full-term (35-37 weeks of gestation), and their development was completely compatible with their gestational age. Two years after their deliveries, the infants, as well as their mothers, remain healthy.

Conclusions: In cases of oligo/anyhydramnios due to amniocentesis during the 16th gestational week, amnioinfusion seems to be able to contribute in reducing the percentage of appearance for major complications, both in fetuses and their mothers. Resulting in a normal pregnancy outcome. A multicentric, prospective, randomized trial with adequate number of patients is necessary, so as to draw safe conclusions on the efficacy and wide application of amnioinfusion.

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Pre- and postnatal therapy of lower urinary tract obstruction – an experience of 18 years

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With prenatal detection of hydronephrosis and technological advances in surgical equipment, the management of lower urinary tract obstruction has evolved to include prenatal surgical intervention. Surgical intervention, was based upon the rationale that restoring amniotic fluid to normal levels by shunting fetal urine from the obstructed urinary system to the amniotic space would prevent lung hypoplasia and, thus, improve neonatal survival. In addition, relief of the obstruction would also reduce back pressure and reduce injury to the developing nephron, thus improving long-term renal function postnatally.

However, this remains investigational, and the vast majority of affected infants are treated soon after birth.

We have experience since 1991 with prenatal treatment of megacystis. In 23 cases of 50 detected megacystis with oligohydramnion in male and without other abnormalities a prenatal intervention by bladderpunction and in 12 cases additional vesicoamniotic shunt placement was performed.

The prognosis of megacystis with oligohydramnion is stated with a survival rate of 10-30%. In our group 54% (13 children) survived.

Also we want present 56 cases of urethral valves with a postnatal transurethral intervention. With a follow up time from 8.6 (3 to 15) years we attend 34 children (60%) with normal renal function, 21% (12) with mild or moderate renal insufficiency and there was a kidney transplantation in 6 cases necessary.

With our multidisciplinary presentation we want to discuss the indication, interdisciplinary aspects, risks and the follow up of pre- and postnatal intervention in such cases.

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Safer cordocentesis by new 25-gauge needles

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Objective: The objective of this study was to establish safer cordocentesis by using newly produced 25-gauge needles rather than the needles currently used. Methods: Human umbilical cords were preserved in experiment 1. Pinching both ends, cordocenteses were performed by filling the cord with saline inside the sphere of the pressure-equilibrated Ringer's solution bag in an aquarium. Pressure alterations were recorded before and after the cordocenteses (n =5 in each needle) using 22-, 23-, and 25-gauge needles. In experiment 2, human umbilical blood after delivery was preserved. Umbilical blood was drawn in syringes, and fixed in syringe infusion pumps of 150ml/h. The blood (n =8) was then pushed into the test tubes through 22-, 23-, and 25-gauge needles. Hemolysis and platelet activation were evaluated. Non-stress tests (NST) subsequent to cordocenteses were compared between 23-gauge (n =19) and 25-gauge (n =16) needles. Results: In experiment 1, the 25-gauge cordocenteses documented a more favorable pressure curve than other needles. In experiment 2, no statistical significance was observed for plasma-free hemoglobin, total bilirubin, hemoglobin, AST, LDH, potassium, platelet count, beta-thromboglobulin, and platelet factor IV. As in the case of clinical data, NSTs subsequent to cordocenteses revealed strong significance in the duration to recover variability (p =0.0003) and the duration to recover acceleration (p =0.0033). Conclusion: We concluded that 25-gauge needles appear superior in avoiding blood loss in the leaking phase. We propose that use of 25-gauge needles is promising under appropriate procedures in cordocentesis.

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Prenatal diagnostic, treatment and postnatal outcome of Megavesica: An interdisciplinary approach

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Background: Fetuses with megavesica are typically diagnosed between 14 and 18 weeks of pregnancy. Oligohydramnion is often paralleling and complicates detailed sonographic evaluation. In early pregnancy it is difficult to estimate fetal kidney function beside normal amniotic fluid production.

Patients: We report on a series of 9 cases with fetal megavesica. First diagnosis was established between 13+5 and 19+6 weeks of pregnancy. All parents were offered interdisciplinary management (neonatology, nephrology), invasive diagnostic testing (amniocentesis, urine analysis) and treatment (shunting, puncture).

Results: 8 pregnancies underwent vesicocentesis (14+5 to 20+0 weeks) for urine analysis (electrolytes, microalbumines, osmolality) before intrauterine shunting was performed. 5 mothers decided to have fetal karyotyping. 2 pregnancies were terminated after vesicocentesis and parental counseling. In 6 fetuses showing at least partial normal kidney morphology a double pig-tail stent (Harrison drain; Cook; Spencer; Indiana; USA) was inserted into the megavesica. Dislocation of the shunt occurred in all fetuses. In one case the parents decided to terminate the pregnancy at 16+2 weeks after dislocation. Replacement of further shunts was performed in 4 fetuses up to 3 times. Delivery took place between 26+0 and 39+6 weeks of pregnancy. Preterm delivery was necessary due to chorioamnionitis (26+0, neonatal death after 10 days), fetal hemorrhage (31+2) and PROM at 34+3 weeks. In one case with 4 insertion of a cook-stent and 2 vesicocentesis' delivery took place at 39+3 weeks.

Discussion: Despite unfavorable prenatal findings and having undergone numerous fetal interventions neonatal outcome may be favorable. Counseling parents therefore is difficult and merits interdisciplinary early approach.

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A case of appendicitis acuta perforativa in an infant

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Introduction: Inflammation of the appendix in children and adolescents is the most common acute surgical state and in most cases it’s easy to handle. Unfortunately, it’s not always the case.

Aim: The aim of this study was to present a case of Appendicitis acuta perforativa in an infant, as well as diagnostic and treatment methods.

Case study: In this study a 42 days old infant was examined. The infant was a Caesarean delivered second twin in the 35th week of gestation with BM=1,900g.

The heteroanamnesis given by the mother appoints that the infant’s postnatal development was normal till the 42nd day, when it became upset and refused breastfeeding. Anemia and leucocytosis was found during the laboratory examination. Antibiotics were administrated parenterally because of suspicion for intestinal infection. Although the infant was treated with antibiotics, paralytic illeus occurred.

The infant with a clinical feature of Abdomen acuta was transferred to the Clinic of Pediatric Surgery where a blood transfusion and operation were carried out. During the operation the patient was diagnosed with Appendicitis acuta perforativa. The operation and the postoperative period were without any complications and the infant was released from hospital ten days after the operation.

Conclusion: Although rarely, appendicitis acuta can occur in infants and it’s generally diagnosed intraoperatively, as seen in this case. Even the most experienced surgeons can often have diagnostic and therapeutical problems handling this particular medical entity.

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Low-dose doxapram for the treatment of apnea of prematurity: A randomized, double-blind, placebo-controlled trial

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Objective: To evaluate the efficacy and safety of low-dose doxapram for the treatment of idiopathic apnea of prematurity (AOP).

Design: Multicenter, randomized, double-blind, placebo-controlled trial with open-label rescue.

Setting: Five neonatal intensive care units in Japan.

Patients: Seventy-two infants with AOP unresponsive to intravenous aminophylline infusion. Gestational ages from 25 to 32 weeks and postconceptional ages less than 33 weeks.

Intervention: Doxapram was administered intravenously with a loading dose of 1.5mg/kg over 1 hour period, followed by a continuous infusion of 0.2mg/kg/h, or placebo, for up to 7 days. Infants failing double-blind therapy could receive open-label rescue.

Results: Apnea more than twice/1 hour or more than 3 times/8 hours or the episode which required mask and bag resuscitation after continuous infusion was defined as treatment failure. Times to treatment failure (TTF) were compared between low-dose doxapram group and placebo group. TTF in low-dose doxapram group was significantly longer than that of placebo group. There were no significant differences in number and percentage of adverse events between groups. There was no serious adverse event in both groups during the study.

Conclusions: Although doxapram has been used for the treatment of AOP as an alternative to methylxanthines, no placebo-controlled trials have been performed to confirm the efficacy and safety. From our study, low-dose doxapram is safe and effective for treating AOP.

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Pulmonary air leak in twin preterm neonates born to a mother with substance abuse

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Introduction: Air-leak syndromes usually occur in infants with poor lung compliance, which are being treated with mechanical ventilation, but may also occur spontaneously. We describe two premature neonates, twin sisters with air-leak syndrome (pulmonary interstitial emphysema, pneumothorax) born to a heroin addict mother.

Case: Two dizygotic female twins, born to a heroin addicted mother, presented air-leak syndrome during ventilation weaning. They were born 28wk of gestation, weighting 1200g and 1000g respectively. Both needed resuscitation. After initial stabilization, surfactant was administered (2doses). On day 7, twin B’s condition deteriorated. Chest radiograph showed a left tension pneumothorax. Thoracentesis was carried out, and a chest tube was placed. On day 10, twin A, became cyanotic while still on ventilation, and her chest radiograph showed a left unilateral pulmonary interstitial emphysema. She underwent left selective bronchial intubation, and high frequency ventilation, nitric oxide were initiated. Her clinical condition and radiological findings improved, and her oxygen requirement decreased. Both twins were discharged. Their chest radiology was that of bronchopulmonary dysplasia.

Comments: The use and abuse of addictive drugs such as opiates, cocaine, nicotine etc. during pregnancy have many adverse affects on the fetus. They freely cross the placenta. Some of the above substances have vasoconstrictive properties. Others reduce lung elasticity, thus reducing lung compliance. It is known that spontaneous pneumothorax may occur during labor in pregnant women, who are heroin addicts. It is possible that prematurity accompanied by their mother’s addiction to heroin, were the predisposing risk factors for the late, spontaneous air leak syndrome in both twin sisters.

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Bacillus spp bacteremia in a term neonate

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Introduction: Despite the widespread distribution of bacillus spp (aerobic spore-forming rods) in nature, they rarely cause infection. They can be pathogenic in immunocompromised hosts. We report for the first time a case of bacillus spp bacteremia in a term neonate

Case: A female neonate, 38 wks of gestation, weighting 3390g was born by caesarean section and Apgar Score 1’-7 and at 5’-8, was admitted to the NICU, with abdominal distention and gastric residue. At day 2, milk was commenced, which she tolerated well. On the 8th day, she looked unwell, became lethargic, and hypotonic. Her condition deteriorated and required Dopamine and FFP transfusion. A full septic screen was carried out. Total leukocyte count 20.180/mm (neutrophils-89%, lymphocytes-6%, monocytes-5%), Hb-12g/dl, Hct-36%, PLT-28,000/mm, CRP-120mg/L. Chest radiograph was normal. Blood culture grew a motile Gram-positive rod, bacillus spp. which was reported as a contaminant. Urine culture was negative. CSF study was negative. Blood culture repeated two days latter continued to grow the same organism. By now, it was apparent that the isolate could not be considered a contaminant. Vancomycin – cefotaxime were started, based on susceptibility pattern. There was clinical and laboratory response to the antibiotics, which she received for a total of 10 days.

Conclusion: Despite the presence of Bacillus spp. in air, soil and dust these organisms have rarely been implicated in human disease. Predisposing risk factors include prematurely, mechanical ventilation and indwelling catheters. We describe a rare case of bacillus spp bacteremia in a term neonate with no predisposing factors.

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New oral therapies for neonatal persistent pulmonary hypertension in newborn with chronic lung disease

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Background Neonatal persistent pulmonary hypertension (NPPH) is characterized by persistently high pulmonary vascular resistance. This condition is often secondary to chronic lung disease (CLD) with chronic pulmonary vascular changes. Although inhaled NO (iNO) therapy and high frequency oscillatory ventilation (HFOV) improved the clinical course and outcomes of many infants, pulmonary hypertension can be refractory to inhaled NO and at HFOV or the dependence of iNO therapy suggesting the need for additional approaches to severe PPHN. Case report We report a case of a girl born at 24 weeks of gestational age with a birth weight of 480gr. She was mechanical ventilated (SIMV) for two months, and after an infectious episode, she has developed oxygen-dependence and severe PPHN (PAP 125mm/Hg). This pathological condition was initially treated with HFOV (MAP 12cm H2O, FiO2 0.7% with SatO2 80%) for 25 days associated with iNO at the dose of 20ppm. Therefore, for non-clinical improvement, the girl was treated with oral Sildenafil at the dose of 2mg/kg/6h and after five days with oral Bosentan 8mg/kg/die. She has presented a significant improvement of clinical conditions 72 hours after starting treatment with sildenafil. The association of Bosentan has been decisive in improving the oxygenation and the echocardiography parameters (PAP 50mm/Hg) and for a gradual weaning from mechanical ventilation. Conclusion Many data are reported in literature about the use of Sildenafil, Bosentan and other drugs useful for the management of NPPH. However, further studies are needed to define the optimal dose, the therapeutic and side effects.

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Correlation of direct antiglobulin test (DAT) with the newborns haemolytic disease and the causes of jaundice

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Aim: To study the direct Coombs test (DAT) in newborns with haemolytic jaundice, in relation to its causes. Material-Method: 49 cases of newborns with haemolytic jaundice that appeared few hours after the labor, were included in the study. For all –newborns and mothers- the blood group as well as the phenotype of the Rhesus and Kell system were examined, while the direct and the indirect Coombs tests were held. In quite many cases of alloimmunization to other antigens and positive IAT, a further control, were carried out.

Results: It was proved that in 32 newborns (65.3%) the jaundice was due to an ABO incompatibility, in 9 (18.4%) to a G6PD deficiency and in 8 (16.3%) there was an alloimmunization of the mother. Positive DAT was found in 7 out of the 32 newborns (21.9%) with ABO incompatibility, and in 7 out of the 8 (percentage 87.5%) with alloimmunization of the mother. On the contrary, none of the newborns with G6PD deficiency had a positive DAT. Conclusions: 1) It was found that the DAT in newborns with haemolytic disease due to ABO incompatibility is positive in a much lower percentage and shows a much lower positivity strength, in comparison to that due to the alloimmunization of the mother. 2) In newborns with coexistence of ABO incompatibility and alloimmunization of the mother, the DAT was found negative. Finally, 3) In all the cases of ABO incompatibility that required a blood exchange transfusion, the DAT was positive.

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New mild type of bronchopulmonary dysplasia

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Major differences between two groups of premature with RDS (one with and the other without BPD) were analyzed (presence of antenatal or hospital infection, surfactant therapy, mode of ventilation, prevention and therapy of BPD). Newborns up to 32 weeks of gestation with RDS in the two year period were analyzed retrospectively. 45 premature were treated for RDS, 42% developed mild BPD. One baby died. Antenatal steroids were given to 30% of newborns. 26% of newborns with BPD got antenatal steroids. Incidence of antenatal infection has been 30% (one third of them developed BPD). Hospital infections had 22% of newborns. One half of neonates with RDS had an infection, and half of them BPD. One third of neonates received surfactant two hours and more after the symptoms of RDS. All of them developed BPD. Only 10% of these with BPD received surfactant on time. Preterm with BPD have been ventilated with SIMV mode (85%) and these without by CPAP (57%), PSV +VG (30%) and SIPPV+VG (13%). 44% of neonates with BPD receive oxygen higher than 40% for more than 5 hours comparing with noon in the second group. Every newborn without BPD received caffeine for prevention. In the other group 52% receive corticosteroids. Incidence of mild BPD can be lowed by antenatal corticosteroids and by better prevention of infections. Surfactant must be given on time, sophisticated modes of ventilation can be used, concentrations of oxygen as low as it can bee. Application of caffeine is helpful.

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Persistent hypothyroxinemia in low birth weight infants detected by neonatal mass-screening (Clinical analysis)

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Background: Our data indicated that hypothyroxinemia without TSH elevation in LBW infants improved gradually after birth. But to identify the infants with thyroid diseases needed LT4 replacement therapy is difficult. Our purpose is to analyze the clinical causes of persistent hypothyroxinemia in LBW infants.

Patients and Methods: Hospital based retrospective study. A total 1094 LBW infants delivered 1995 to 2005 in Kitasato university hospital were induced. Neonatal mass-screening (MS) measured both TSH and FT4 simultaneously were performed around fifth days after birth primarily, and about one month after secondly. Then the medical records were sorted out four clinical causes of persistent hypothyroxinemia, including cretinisms, maternal thyroid dysfunctions, iodine contaminations and seriously ill conditions.

Results: Four infants with cretinism, nine with maternal thyroid dysfunction, 26 with iodine contaminations and 21 with serious illness were detected. Two of four preterm infants with cretinism showed normal TSH levels in primary screening and delayed TSH elevation. Two of nine infants with maternal thyroid dysfunctions showed persistent hypothyroxinemia and were treated with LT4. Twenty six infants with iodine contamination showed low FT4 levels (1.15±0.80ng/dl) compared with non-contaminated infants (1.40±0.67ng/dl, \(p=0.002\)). Twenty one infants died within 30 days after birth with serious illness showed marked low FT4 levels (0.53±0.47ng/dl) without TSH elevation.

Conclusions: MS for cretinism of LBW infants should be performed repeatedly. Maternal thyroid disease, iodine contamination and serious underlining diseases should be considered in LBW infants with persistent hypothyroxinemia.

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Clinical and biological study of necrotizing enterocolitis

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Background The necrotizing enterocolitis (NEC) represents a frequent death cause in VLBW. The authors intend to determine the prevalence of the risk factors and the clinical forms of the disease.

Methods We studied 103 cases of the premature newborns with NEC (3.24%), hospitalized in Neonatal Department, between 2002–2008.

Results The disease frequency has been greater at premature newborns with gestational age <32 weeks and birth weight <1,500 grams (78/103). The enterocolitis could be related to an abnormal pregnancy and birth: premature rupture membrane in 15.62%, colored amniotic liquid in 26.56%, abnormal birth in 28.12%, APGAR score less than 5 in 53.12%. The frequent clinical signs were: diarrhea in 91%, abdominal distension in 78%, hemorrhagic stools in 76%, vomiting in 71%, transitory apnea in 59%, thermic instability in 58%, edema of the abdominal wall in 34%, hemodynamic disturbances in 29%.

The evolution was towards healing due to medical therapy in 23.43%, due to surgical therapy in 14.06% and to deaths, in 54.68%.

Conclusions: In our study, the risk factors of the NEC are: low birth weight, prematurity, severe asphyxia at birth correlated with pathological birth circumstances, intensive therapy needs at birth, infectious factors.

Necrotizing enterocolitis remains one of the most common emergencies in newborn infants because of the bowel perforation.

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Experience with biochemical diagnosis of inherited amino acid disorders

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Assay of total as well as individual amino acids level in biological fluids has become an increasing practice in laboratory medicine. While the total amino acids content of plasma and urine is expected to reflect the nutritional/metabolic status, the individual amino acids profile of biological fluids are of importance in confirming or otherwise to rule out the suspected amino acidopathies. The present study presents amino acids profile for some of the rare amino acidopathies.

Amino acid analysis in physiological fluids was performed with ana Biochrom 30 amino acid analyzer, using ninhydrin as a derivative agent. The method provides a comprehensive profile of 53 amino acids in a single run lasting 120 minutes. With this methodology we were able to confirm the diagnosis of varieties of amino acidopathies such as phenylketonuria, homocystinuria, cystinuria, histidinemia, tyrosinemia, citrullinemia, ornithine transcarbamylase deficiency, maple syrup urine disease and non-ketotic hyperglycinemia.

Inherited amino acid disorders for patients with clinical suspect diagnosis in years 2005 to 2009 (800 patients) including the following: cystinuria (12 cases), homocystinuria (4 cases), maple syrup urine disease (1 case), non-ketotic hyperglycinemia (2 cases), tyrosinemia (2 cases), citrullinemia (1 case), hyperprolinemia (1 case), phenylketonuria (24 cases).

Availability of such facilities in pediatric care centers, by way of an early diagnosis and therapeutic intervention may help in prevention of irreversible damage and attenuation of clinical severity of the disorder. In certain instances where therapeutic intervention is not feasible, confirmed diagnosis could help in genetic counseling and prenatal testing.

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Trimethylaminuria as challenge for screening in pediatrics and neonatology

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Introduction: Trimethylaminuria is only occasionally identified during childhood and infancy. Some children with trimethylaminuria have a strong odor all the time, but most have a moderate smell that varies in intensity over time.

Methods: Measurement of urine for the ratio of trimethylamine to trimethylamine oxide is the standard screening test. The plasma samples were analyzed for TMA using SPME and GC–MS.

Results: The analysis of the effect of dietary treatment on amine metabolism and distribution was extended to studying urinary biogenic amines. The concentrations of TMA in plasma (1.50±0.50 µM) were significantly (P<0.05) higher than the corresponding levels in healthy childrens (0.40±0.15 µM).

Discussion: The outstanding biochemical feature in the fish malodor syndrome is the excessive excretion in the urine of un-oxidized trimethylamine. A number of factors have been proposed to explain TPN-related effects on gastrointestinal and hepatic function including modulation of gastrointestinal peptide hormones.

Conclusion: Trimethylaminuria has an autosomal recessive pattern of inheritance. Trimethylamine (TMA) is a volatile short-chain aliphatic amine that has the characteristic odour of rotting fish. Flavin-containing monooxygenase 3 is also known to be involved in oxidative detoxification and metabolism of several substances and drugs; thus, its enzyme variability is considered to have metabolic and clinical implications beyond body malodor.

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Hypothermia in HIE neonates – implementation of the clinical procedure into the German health care system

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Procedure: Hypothermia is used in asphyxiated neonates born at term in NICU settings. At 6 hours post partum, the children are kept at 32-34°C Celsius for 72 hours.

Health Technology Assessment: RCTs evaluated in a 2007 Cochrane Review so far indicate benefit in mortality without increasing the number of impaired survivors. At the moment there are 3 more studies to be published to hopefully confirm this stimulating Result. Nevertheless, there are still a lot of clinical questions to be addressed: i.e. how to cool (choice of appropriate equipment), preferred protocol, co-treatment, level of perinatal care

Implementation into G-DRG: Once the clinical aspects are settled, the aspects of reimbursement have to be regarded. The German Social Law allows hospitals to freely implement innovations, nevertheless these should be considered adequately in the reimbursement system, G-DRG in this case. At the moment hypothermic treatment only gets sufficient remuneration, when coded with 95 hours of artificial ventilation, which is not necessary in all cases. So a proposal has to be developed in order to find a better description for the procedure in G-DRG.

Quality assurance: Last not least a protocol has to be implemented to describe the procedure correctly and make sure, that every hospital using hypothermia adheres to it. Treatment Results then could be compared and help to establish GCP.

Institutions involved: The presentation/poster will demonstrate how many hands are involved to implement the procedure from clinical studies into the German Health Care System

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Criteria for intubation and mechanical ventilation in infants on NCPAP

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Introduction: Despite the acknowledged clinical usefulness of NCPAP, uncertainties regarding aspects of its application remain.

Objective: To determine early predictors of NCPAP failure and optimal criteria for mechanical ventilation (MV).

Materials and methods: A retrospective cohort study of 74 newborn infants admitted to the NICU of our Center and initially treated with NCPAP was performed. The infants were divided into 2 main groups (I- 56 patients with effective NCPAP, II- 18 babies who required MV). We compared dynamics of clinical signs (Respiratory Rate (RR), Silverman/Downes score), parameters of NCPAP and laboratory data (pH, PaO2, PaCO2, Oxygenation Index (OI), and alveolar-arterial oxygen tension difference (A-aDO2) between 2 groups at 1, 3, 6, 12, 24 and 36 hours of life.

Results: The demographic compositions and initial signs of respiratory failure were comparable. From 3-6 hours of life, the Silverman/Downes score and RR were significantly higher in group II (2.3±1.4 and 65±16 in group I vs. 3.6±1.7 and 77±17 in group II). By 6 hours, a difference in FiO2 and MAP appeared. A significant difference in OI and A-aDO2 between the two groups appeared only at 12-24 hours of life. We did not find significant difference in the dynamics of pH, PaCO2 and PaO2.

Conclusion: Our Results show the first predictors of NCPAP failure to be clinical signs (increasing RR and Silverman/Downes score) and parameters of NCPAP. The laboratory data can not be considered as early predictors and optimal criteria for intubation as they depend on compensatory abilities of each patient and become indicative of NCPAP failure much later in time.

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A torsioned and autoamputated ovarian cyst in the fetal period: A case report

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Aim: We report a case of a torsioned and autoamputated right ovarian cyst.

Material and methods: A 28 year old primigravida in 33+5 weeks of gestation, was addressed to our Department.

Results: A large, complex cystic lesion is seen within the lower abdomen of the female fetus, measuring 52x42x32mm. No other gross fetal anatomic abnormality was seen. The patient was delivered in the 39 week of gestation (50/3100/9). The postnatal ultrasound confirmed a cystic mass in the right upper quadrant. Surgical treatment was decided. Intraoperatively, the ovarian cyst was found to be autoamputated and was adhered to the antimesenteric edge of the ileum by a fibriotic band.

Discussion: Almost all ovarian cysts are benign corpus luteal cyst of germinal or graafian tissue origin, which is not a real neoplasm. Cysts do not develop before the 23 week of gestation, since they are caused by maternal hormonal influence on the maturing fetal ovaries. Prognosis is generally excellent. Most cysts spontaneously resolve without postnatal treatment. The most serious complication of fetal ovarian cysts is torsion. Partial or complete rotation of ovary on its pedicle, compromising first lymphatic, then venous, and arterial flow, leads to hemorrhagic infarction and to loss of the ovary. In our case a healthy baby girl was born without clinical and sonographic evidence of ovarian torsion. This finding can be explained by autoamputation of the cyst.

Conclusion: Prenatal ultrasonography allows diagnosis of fetal ovarian cysts and may suggest antenatal complications.

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**Persistent hypothyroxinemia in low birth weight infants detected by neonatal mass-screening (Basic analysis)**

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**Background:** Evaluation and treatment of central hypothyroxinemia in LBW infants remains unclear.

**Purpose:** To analyze the distributions and changes of FT4 and TSH levels after birth in LBW infants.

**Patients and Methods:** A hospital-based retrospective study. A total 1094 LBW infants (<2000g) delivered from 1995 to 2005 in Kitasato University Hospital were induced to this study. Neonatal mass-screening measured both FT4 and TSH simultaneously were performed 4 to 10 days after birth and about one month after birth again in LBW infants (<2000g).

**Results:** Mean FT4 levels (BBW(g):<800/ <1200/ <1600/ <2000=FT4: 0.46±0.37/ 0.96±0.56/ 1.43±0.57/ 1.72±0.57ng/dl, GA(wks):<28/ <32/ <36/ <40=FT4: 0.56±0.42/ 1.08±0.49/ 1.62±0.52/ 2.03±0.51ng/dl) were significantly low in VLBW infants without TSH elevation (BBW(g): <800/ <1200/ <1600/ <2000=TSH: 4.52±5.87/ 4.27±4.25/ 3.93±3.09/ 3.95±2.90µU/ml, GA(wks):<28/ <32/ <36/ <40=TSH: 4.14±4.76/ 4.02±4.41/ 3.87±2.31/ 4.44±3.11µU/ml). FT4 levels correlated positively with BBW and GA (p<0.001). One month after birth FT4 levels in VLBW infants were increased but still low compared with those of more matured infants.

**Conclusions:** Central hypothyroxinemia was persisted more than one month after birth in VLBW infants. We should consider how to screen the infants with pathological hypothyroidisms that needed LT4 replacement therapy.

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Parametrial hernia mimicking uterine rupture
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Uterine rupture during pregnancy is a rare, but potentially life threatening event, for both the mother and the fetus. Uterine dehiscence implies the disruption of all uterine layers including the serosa. Uterine rupture, involves the tearing of all uterine wall layers associated to acute fetal distress, severe bleeding and the expulsion of membranes and/or the placenta. It is strongly related to previous surgeries; most commonly caesarean sections or myomectomies.

The site of rupture is usually the uterine caesarean scar. The tearing of this avascular section of the myometrium, is associated with a better outcome than those occurring in the lateral section, which might include the uterine artery or any of its branches.

In the following case, we present an enteric parametrial hernia mimicking the image diagnosis of a uterine rupture. The patient's history of a previous parametrial surgical repair, and the coinciding location of the image, reinforced the misapprehension.

Basing a diagnosis on imaging methods only, without considering the concomitant clinical findings; harbors the risk of performing erroneous obstetrical interventions which may jeopardize the health of both the mother and the fetus.

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Pelvic cyst: Not always an ovarian cyst

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Introduction: We present a case of hydrometrocolpos, associated with a persistent cloaca.
Clinical report: A pregnant women, 35 years-old, was referred to our centre at 32 weeks for a fetal ovarian cyst. A cystic mass was confirmed (99x83x67mm), probably arising from the left adnexa. A bilateral pyelectasis was identified. Ultrasound-guided puncture was performed (280 mL). Estradiol, progesterone and testosterone levels were below those expected for an ovarian cyst. Fetal karyotype was 46,XX. Cytologic examination disclosed squamous cells. At the next day, the cyst had refilled and the hypothesis of a rectal dilatation arose.
MRI showed a pelvic cyst where both ureters ended; the bladder presented a normal morphology but was slightly distended; neither the uterus nor the rectum could be identified.
A HELLP syndrome developed at 33 weeks and caesarean-section was performed. The newborn had an Apgar score of 2/4/4 and 2000g, and presented besides the pelvic cystic mass, ambiguous genitalia, anal atresia and small anterior fistula. The cyst was punctured (200 mL) and the newborn died 2h after birth.
A necropsy examination was performed. The diagnosis was “persistent cloaca” in a female newborn: very dilated uterus and vagina, as well as a dilated bladder, were both ending in an elongated urethra-like cloaca. Also seen rectal atresia with a small non-functioning fistula to the uterus and a hypoplastic anus. Furthermore there was “borderline” pulmonary hypoplasia.
Conclusions: Prenatal diagnosis of hydrometrocolpos is difficult; MRI can be very helpful, but in this case the diagnosis was only made by autopsy.

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The contribution of perinatal bloodparameters in the early detection of fetal distress

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Aim: The determination of pH –fetal scalp, base excess (BE)- fetal scalp, pH –umbilical cord artery, BE- umbilical cord artery, especially in cases of pathological cardiotocographic findings, has been established as a useful and reliable method to early detection of fetal distress. Method: In a retrospective study between 2004 and 2006 in our Department, we investigated the reliability of the above parameters during active labor in 100 women with the appearance of variable or late decelerations in cardiotocography. Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS), version 16 (SPSS, Inc., Chicago, IL, USA). All tests were two tailed and statistical significance was considered for p values less than 0.05. Results: The mean age of our study-participants was 27.9 years (min 19, max 42, SD 5.96). The mean gestational age of their pregnancy was 40.1 weeks (min 36, max 42, SD 1.25). Out of the 100 women, 59 gave birth with normal labor, 27 had a Caesarian section, 10 had a forceps delivery, while the remaining 4 had an emergency Caesarian section. We investigated correlations of the combinations of fetal scalp- and umbilical cord parameters-measurements with the Apgar scores. We found a statistically significant correlation between fetal scalp BE (r=0.263) with Apgar scores 1΄, umbilical cord BE (r=0.314) with Apgar scores 5΄, and umbilical cord pH (r=0.387) with Apgar scores 10΄. Conclusion: The intrapartum blood-examination should be included both parameters (pH and BE) in the correct management of labor.

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A case of prenatally diagnosed arachnoid cyst with low PAPP-A and elevated free B-HCG

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Introduction: Arachnoid cysts represent collections of cerebrospinal-like fluid enclosed within layers of pia arachnoid.

PAPP-A (Pregnancy-Associated Plasma Protein A) is a glycoprotein. When measured between the 11th and 14th week of pregnancy (combined with $\beta$-HCG) it is mainly used as a marker to access the risk of chromosomal anomalies.

Aim: To present a case of a prenatally diagnosed arachnoid cyst at 34 weeks of gestation associated with low PAPP-A and elevated free $\beta$-HCG at 13 weeks of gestation.

Case Presentation: A 39 year-old woman presented at 13 weeks singleton gestation with low PAPP-A (0.34MOM) and elevated free $\beta$-HCG levels (1.34MoM). Amniocentesis revealed a normal male karyotype 46 X,Y. Initial prenatal ultrasound scan was normal but subsequent scan at 34 weeks gestation revealed a large cyst in the right middle cranial fossa (4.5cmx3.17cm). Fetal brain MRI confirmed the diagnosis of a right middle cranial fossa arachnoid cyst. A male infant was delivered by caeserian section with no other congenital anomalies present. Findings of postnatal brain MRI were consistent with the above diagnosis.

Discussion: Little is known about the antenatal natural history of arachnoid cysts. Two cases of arachnoid cysts have been described in literature associated with increased maternal serum a-fetoprotein. In our case of prenatal arachnoid cyst PAPP-A and $\beta$-HCG at 13 weeks gestation were abnormal. To our knowledge this is the first reported case of an arachnoid cyst associated with an abnormal PAPP-A and $\beta$-HCG levels at 1st trimester of pregnancy.

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Partial hydatidiform mole with 17 weeks alive fetus associated to pre-eclampsia

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Primiparous with normal course pregnancy started at 17 weeks with migraines, vomits, abdominal pain, dyspnea and edemas in lower extremities. High blood pressures was registered (152/102). We observed by ultrasounds an alive fetus according to the gestational age with a defect in the anterior abdominal wall (omphalocele) and many pooling blood in placental structure. We also found analytical alterations: proterinuria (24 hours) 2,560mgs, GOT 68 U/L, GPT 80 U/L, LDH 527 U/L, 119 x103 platelets and 318,641 β-hCG mIU/ml. Due to the worsening of the clinical course with an elevation of arterial blood pressure that requires antihypertensive intravenous treatment and magnesium sulfate with intensive monitoring, as well as evident congenital malformation and high suspecting of serious placental disease, we decided to interrupt the gestation by maternal interest. Polyploidy 69XXX and mola partial were confirmed by the histological and cytogenetic study. The patient developed favorably, all of the analytical parameters came back to the normality and She was discharged 48 hours after the uterine evacuation.

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Prenatal diagnosis of defects in the abdominal wall and postnatal development: Gastroschisis

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Introduction: Gastroschisis is defined as a paraumbilical defect of the abdominal wall, usually on the right cord, which leads to extrusion free (not covered) of intraabdominal viscera, especially intestine. The prevalence ranges from 0.3-0.9/10.000, describes a remarkable increase in recent years. The prognosis depends primarily on neonatal intestinal conditions at birth and maturity of the lung.

Materials and Methods: We study and follow up of 6 cases of gastroschisis since 2003

Results: the diagnosis was made by antenatal ultrasound in 83% of cases. The key finding is the presence of intestinal loops floating in the amniotic cavity with a membrane that covers and it is not uncommon view is that obstruction of the bowel into the abdominal cavity, objectifying hidramnios partner. The immediate postoperative complications, mainly sepsis were early (<72 hours) (3 cases), late sepsis (>72) (3 cases), renal (3 cases), intestinal obstruction (2 cases) and septic shock with multiorgan failure (1 case). The survival group was 86%.

Conclusions: Ultrasound is the primary tool for prenatal diagnosis and monitoring of patients with gastroschisis. 100% of the cases have exposure of intestinal loops, but it is possible to find the evisceration of colon, stomach, gallbladder, liver and gonads, and bladder and less frequently. Ultrasound has also been used to define fetal prognosis based largely on the following sonographic parameters, which are designed to detect early gastrointestinal complications: dilatation of bowel loops, bowel wall size, and volume of gastric dilatation amniotic fluid, mesenteric Doppler.

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Appearance of gestational diabetes in the greek prefecture


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Aim: The of Gestetional Diabetes (GD) was investigated in Greece Prefecture.

Material – Method: 364 pregnant women (age 23 up to 41 years) were submitted in ordeal of tolerance of glucose in the frames of preventive progenetic exams. The examination became between 24th and 28th week of pregnancy after 12 hours fast. Firstly, it was given by oral administration solution 75gr of glucose diluted in 300ml of water and was followed blood takings in interval 1, 2 and 3 hours. The determination of glucose value became in biochemical analyst with enzymic method. It is marked that no one pregnant women reported historical of diabetes.

Results: 22 pregnant women (5.04%) had pathological Results. At least two measurements presented pathological values (glucose value in fast >126mg% and glucose value 2 hours after reception of glucose >200mg%).

Conclusions: 1) The percentages of GD remain high. 2) The diagnosis of GD allows to be investigated the pathogenesis and to be applied the proper prevention - treatment, so as to be deterred the unfavorable development of the illness. 3) In order to avoid the serious consequences to the infant, to the future growth of child, but also to the mother, the preventive control for GD should be applied in all pregnant. It is the only way to find out any problem.

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Fetal toxic effects of angiotensin II type 1 receptor antagonists: Case report

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Administration of angiotensin II type 1 receptor antagonists (ARA) during the second trimester of pregnancy is known to cause fetal abnormalities. We report two sibling cases. In the second case candesartan (an ARA) had been given to the mother for several years because of primary hypertension. The medication was stopped at 22 weeks’ gestation when severe oligohydramnios was noted and when the kidneys’ structure appeared to be severely affected. After cessation of candesartan fetal renal function improved as evidenced by increasing amniotic fluid volume, fetal growth approached the normal range. The child was born at 35 weeks of gestation and showed intrauterine growth restriction, renal insufficiency and hypoplastic skull bones. Two years before when on the same anti-hypertensive medication throughout pregnancy, the patient had given birth to a child at 33 weeks of gestation in a different hospital. The child died on the first day of life due to severe perinatal asphyxia. Autopsy revealed pulmonary hypoplasia, skull bone hypoplasia and contractures of the lower limbs.

The fetal abnormalities, which are similar to those observed after exposure to angiotension-converting enzyme inhibitors, are probably related to reduced fetal kidney perfusion that may Result in oligohydramnios and neonatal renal insufficiency.

Conclusion: Angiotensin II type 1 receptor antagonists should be avoided throughout pregnancy at least during the 2nd and 3rd trimester. If these agents are prescribed accidentally monitoring of the amniotic fluid volume after discontinuation of the ARA is highly recommended.

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Prenatal diagnosis of multiple acyl-CoA dehydrogenase deficiency

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Prenatal diagnosis for some organic acidemias is well established and know to be reliable but for some disorders there is less experience and the prenatal diagnosis may be experimental. Multiple acyl-CoA dehydrogenase deficiency (MADD) caused either by deficiency of the α- or β-subunit of electron transfer flavoprotein (ETF) or deficiency of ETF dehydrogenase is an autosomal recessive inborn error of metabolism. Each of these protein deficiencies leads to abnormal function of multiple acyl-CoA dehydrogenases, and thus to abnormal β-oxidation of fatty acids and metabolism of branched-chain amino acids. Affected individuals demonstrate increased excretion of glutaric acid, together with metabolites of the substrates of other blocked acyl-CoA dehydrogenases. We report our first experience with biochemical approach based on quantitation of specific organic acids and acylcarnitine esters in amniotic fluid to prenatal diagnosis at 17 weeks of gestation in a young, Serbian, non-consanguineous couple with a proband affected by MADD. Quantitative assay of glutaric acid performed by capillary gas chromatography showed normal value for 17 weeks of gestation. Quantitative assay of butylcarnitine (C4), isovalerylcarnitine (C5), hexanoylcarnitine (C6), octanoylcarnitine (C8) and glutaryl carnitine (C5DC) performed by tandem mass spectrometry also showed normal values. The pregnancy was allowed to continue and the mother was delivered healthy female baby.

In conclusion, MADD prenatal diagnosis should be performed using biochemical approach, with regard to available information and technologies.

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The markers of alternative action of tobacco smoke in pregnant: Endothelin-1 and nitric oxide

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The purpose of the work was to assess the degree of vascular endothelium damage in smoking pregnant women. The study involved 30 pregnant aged 29.8±1.340, of them 20 smokers with intrauterine growth retardation syndrome and 10 who were not exposed to tobacco smoke with normal pregnancy course. The fact of tobacco smoking was verified by qualitative determining blood serum thiocyanates. At 25-30 weeks of gestation, blood concentration of s-nitrosothiols (s-NO), stable metabolites of nitric oxide, was assessed using fluorometry and that of endothelin-1 (E-1) – using IEA. Blood s-NO amount in pregnant was 0.427±0.014 mmol/l, in smokers – 0.151±0.018 mmol/l (p<0.001). A strong inverse correlation (r =–0.86) was established between blood thiocyanate amount (i.e. smoking intensity) and s-NO amount.

The findings of E-1 amount in the women (non-smokers 2.39±0.19 pg/ml vs. 11.948±2.181 pg/ml in smokers, Å²<0.01) allowed to find a positive medium correlation between this parameter and smoking intensity. A dramatic increase in E-1 amount in the smokers with simultaneous reduction of nitrosothiols concentration suggests endothelial dysfunction due to a damaging effect of toxic products of tobacco in the blood vessels.

A poor negative correlation (r =–0.62) was revealed between s-NO and E-1 levels in the investigated women, which allows to conclude about different degree of influence of alternative factors on production of these substances. This stimulates continuing the study of causative association between them and intrauterine growth retardation syndrome.

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Fetal ventriculomegaly associated to pyruvate carboxylase deficiency: A case report

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Introduction: The incidence of isolated mild (10-14.9mm) fetal ventriculomegaly is 1.4 to 20 per 1000 deliveries. Pyruvate carboxylase deficiency (PCD) is a rare autosomal recessive metabolic disease that cause developmental delay and its incidence is 1 in 250,000 births. Most patients die within the first six months of life. The association of fetal ventriculomegaly and PCD is very uncommon and no cases are described in the literature.

Case report: 32 years-old primigravida with no personal pathological history. Correct gestational control until 27th weeks of gestation, when an isolated ventriculomegaly of 11mm was found by ultrasound. A MR was performed with the diagnostic of mild ventriculomegaly with lateral ventricles at the level of the atria of 12 and 13mm. The rest of neurological structures were normal. No other morphological abnormalities were found.

At 41st week of gestation was born a female newborn, Apgar 9-10, who went into Neonatal Unit at 24 hours of life because of severe metabolic acidosis. She died the 5th day of life. The muscle biopsy diagnosed pyruvate carboxylase deficiency.

Discussion: PCD is a rare autosomal recessive metabolic disease, which Results in malfunction of the citric acid cycle and gluconeogenesis, and thus, in a metabolic acidosis. It is associated with severe lethargy, poor feeding, vomiting, and seizures, and, in the most severe form, in developmental delay, poor muscle tone and abnormal eye movements.

Prenatal diagnosis is really difficult. The association with isolated mild ventriculomegaly is very infrequent. Here remains the interest of this case.

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Effect of prophylactic indomethacin on renal and intestinal blood flow in extremely low-birth-weight infants

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Background: Indomethacin leads to a decrease in renal and intestinal blood flow. The purpose of this study is to investigate the effect of prophylactic indomethacin for intraventricular hemorrhage (IVH) and patent ductus arteriosus (PDA) on renal and intestinal blood flow in extremely low-birth-weight infants (ELBWIs).

Method: Twenty-four ELBWIs were admitted to our hospital and enrolled in a multicenter randomized controlled trial for IVH and PDA. Six-hour continuous infusion of indomethacin (0.1mg/kg) or placebo was started within 6 hours after birth. Nineteen of the infants had no congenital abnormality and were examined by ultrasound before and within 6 hours after administration. We analyzed the 19 infants’ data on renal artery (RA) and superior mesenteric artery (SMA) blood flow, as measured by pulsed Doppler ultrasound.

Results: Gestational age was 22-27 weeks (median 25.5 weeks) in the indomethacin group (n=10) and 24-28 weeks (median 26 weeks) in the placebo group (n=9). The indomethacin group had significantly lower birth weight than the placebo group (528-936g (median 677g) vs. 692-946g (median 800g), respectively). Compared with pre-administration values, post-administration end-diastolic blood flow velocity (EDV) was significantly lower in the left pulmonary artery and significantly higher in the RA and SMA of the indomethacin group. RA and SMA blood flow velocity did not significantly change in the placebo group.

Conclusion: Prophylactic indomethacin appears to lead to an increase in EDV in the RA and SMA via a decrease in ductal shunt volume.

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Prenatal diagnosis of fetal adrenal mass

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Introduction: The use of ultrasound screening for structural fetal malformations has increased the diagnosis of prenatal adrenal masses. The differential diagnosis includes adrenal haemorrhage, renal cysts, teratomas, kidnappings lung, intestinal duplication and neuroblastoma. It should be confirmed in the postnatal period.

Materials and methods: pregnant 34-year-old, primigravida. Total thyroidectomy, hyperprolactinemia, Hodgkin's lymphoma at age 19. Ultrasonography of the 2nd quarter: ecogenic mixed mass of 2.3 x 2.1cm, which depends on the left adrenal gland. NMR: 1.6cm cystic lesion in left adrenal region suggests adrenal hemorrhage versus cystic neuroblastoma. The mass does not vary in size and ecogenic during pregnancy. At week 39 get a female newborn (forceps) of 3,450 grams, Apgar score 10/10. Ultrasound and NMR of the newborn: multicystic left adrenal mass has increased in size. For 15 days of life, left adrenalectomy was performed with suspicion of congenital neuroblastoma. Pathology reports paradrenal mature teratoma.

Results: teratomas are tumors containing germ tissue and variable degrees of differentiation. Neuroblastoma is a malignant extracranial solid tumors more common in children. Ecoestructure have a mixed stable. There are cases of spontaneous regression, which raises questions about early treatment or observation. Adrenal hemorrhage has a favorable prognosis and a spontaneous resolution postpartum.

Conclusions: prenatal sonographic findings of an adrenal mass creates a diagnostic and therapeutic dilemma, because they do not differentiate between benign and malignant. In tumors with favorable clinical and biological characteristics, recommended approach.

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The significance of external cephalic version after 36 weeks of gestation

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Introduction: Views on external cephalic version have passed through a variety of opinions and at present it is becoming much favored. In the interest of maximum safety, it is necessary to ensure that the criteria of the correct indications and procedures are met.

Objective: The evaluation of successful achievements and the safety of external cephalic version after 36 weeks of gestation. The evaluation of factors influencing the accomplishment of external cephalic version after 36 weeks.

Methods: A retrospective analysis of external cephalic version attempts performed on a group of 197 singleton breech pregnancies after 36 weeks gestation in the years 2003 – 2008 at the Department of Gynecology and Obstetrics, Masaryk University, Brno, the Czech Republic. The effectiveness, number and type of complications, and possible influencing factors were observed (placental position, amniotic fluid volume, parity, gestational age, type of breech presentation, estimated fetal weight).

Results: The effectiveness of external cephalic version from breech to head presentation was 32.4%. The number of complications did not exceed 1%. The main factors influencing accomplishment of external cephalic version are gestational age, amniotic fluid volume and estimated fetal weight.

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Fetal magnetocardiogram of a case with non-immune fetal hydrops of non-cardiovascular origin

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Non-immune hydrops fetalis is defined as the presence of excess fluid in two or more body areas such as the abdomen, thorax, or skin excluding the immune etiology. Major causes of non-immune fetal hydrops are fetal heart diseases and chromosomal abnormalities. Mortality from hydrops fetalis is rather high, and its etiology is often unknown. In spite of accumulated reports in fetal magnetocardiograms (FMCG) of heart diseases, FMCG of fetal hydrops of non-cardiac origin has been seldom reported. We reported herein a case of fetal hydrops of non-cardiac origin. The case was referred to us due to fetal ascites and polyhydramnion. The karyotype was 46, XX. Coproporphyrin and virus culture of fetal ascites were negative. Ultrasonography revealed no fetal cardiovascular anomaly. FMCG was recorded for 2 min at 30 wks gestation using 64 channel SQUID system. Raw sequential FMCG recording after the filtering and removal of maternal signals showed no arrhythmia. Averaged FMCG triggered at R waves revealed a prolonged QTc of 435 ms, which was slightly longer than the standard QTc value. The infant was born at 38 wks with a small amount of ascites, which disappeared within 2 wks after birth. The final diagnosis of fetal hydrops was idiopathic. A fetus with non-immune hydrops of non-cardiac origin might show a prolonged QTc, which is related to sudden death and is difficult to diagnose antenatally.

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Intra-amniotic thyroxine in the treatment of fetal goitrous hypothyroidism – case report

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Introduction: Women with Graves' disease who are treated with antithyroid medication during pregnancy are at increased risk of having a fetus affected with goiter.

Case: A 23-year old primigravida with hyperthyroidism due to Graves' disease remained uncontrolled during pregnancy despite treatment with propylthiouracil. At 36 weeks an anterior, bilobed, heterogeneous cervical mass, compatible with fetal goiter, was detected and she was referred to our tertiary care hospital. She exhibited a diffuse goiter and exophthalmym. Ultrasound confirmed the presence of fetal goiter (4.5cm transverse diameter; 10.3cm circumference) with predominant peripheral vascularization and no fetal tachycardia or signs of impending heart failure – findings consistent with fetal hypothyroidism. Iatrogenic hypothyroidism caused by antithyroid drug was strongly suspected and propylthiouracil was kept at 250mg/day. L-thyroxine (300 mcg) was administered via intra-amniotic injection at 37 weeks. Six days later, a decrease in thyroid dimension (38mm transverse diameter) and Doppler pattern of vascularization were demonstrated. Cesarean section was performed at 38 weeks. Goiter was not clinically evident at birth but the laboratorial study confirmed a neonatal hypothyroidism despite high titers of maternal stimulating antithyroid antibodies. Rebound hyperthyroidism developed at day 6 and at day 42 the thyroid function normalized (under treatment with metimazol). The mother was submitted to thyroidectomy four months after labor.

Discussion: Prenatal diagnosis of fetal thyroid dysfunction facilitates adjustment of maternal therapy or, if necessary, in utero fetal therapy. Doppler examination of fetal thyroid proved to be useful in the diagnosis of fetal hypothyroidism in this case.

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The vaginal delivery of a macrosome (5,740g) baby by an untreated gestational diabetic mother

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History and Findings: A 26-year-old pregnant woman (III/G/IP) presented at the antenatal care clinic with rupture of membrane and regular contractions at 39+1 gestational weeks. No anamnestic risk factors were noted in the patient's file. Clinically a glucosurie was noted, but not investigated. Estimated birth-weight by ultrasound was 3800g.

After 6 hours the patient was fully dilated and the head was born with a mediolateral episiotomie. Due to a shoulder dystokie that could not be resolved with the McRoberts maneuver, a manual arm loosening was performed. Simultaneously the pediatricians and anaesthetists were informed about the delivery and were present at the birth of the body.

The male newborn had marked macrosomia (birth-weight 5740g), pH in the umbilical artery was 7.28, Apgar was 0/6/8. Absence of heart beat and of spontaneous breathing required resuscitation.

The maternal HbA1c level was normal.

Fetal Treatment and Course: Echocardiography revealed a hypertrophic ventricel septrum. Neurological deficency in the right arm due to a plexusparesis. No Hepatosplenomegaly. The blood sugar levels were stable with 12 feeds a day, physiotheraphy for the plexus paresis was started. Due to elevated infectious parameters a 3 day antibiotic course was given.

Mother and child were discharge 7days after delivery. The follow up 5 months later showed a healthy baby (9.650g), normal ventrikelseptum and a regression of the plexusparesis.

Conclusion: Undiagnosed and therefore untreated severe gestational diabetes may have fatal consequences for the fetus. Expert committees of obstetricians and diabetes specialists have recommended blood glucose screening between 24-28 weeks of gestation of every pregnant woman as part of the routine prenatal care.

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Syndrome of hyperexcitation of ovaries, case report

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Aim: The presentation of a case with syndrome of hyperexcitation of ovaries as well as its complications.

Material-method: Woman of age of 29 years, with seven automatic and one artificial abortion from her obstetric background and bicornous uterus from the salpingography, was submitted in oocyte retrieval and embryotransfer and the next day arrived in the Obstetrics-Gynaecological Clinic of General Hospital of Pirgos reporting fever, vomiting, intense abdominal ache at the hypogastrium and abdominal dysphoria.

Results: The patient received IM therapy with human menopausal gonadotrophin 75IU, initially 2 daily increasing progressively up to 8 daily. Ovulation was achieved iatrogenic with administration of BCG. At the ultrasound control the ovaries were showed enlarged. The endometrium was portrayed thin and echogenic. There was any embryo sac. At the clinical examination the blood pressure was 120/70mmHg, the pulsation 82/min, the temperature 37.8, the abdomen was mild divaricated and at the percussion there was present the ballottement point. Also there was marked leukocytosis (WBC26x10^3 µL) and hypoalbuminemia (5.7g/dL).

She was placed in supporting treatment within travenous administration of antibiotics (kefouroxim), with parallel hydration and Human Album in up to her last day of hospitalization. The leukocytes increased until 44x10^3 µL, the CRP until 1.3mg/dl, there was presented hyponatraemia, hyperuricemia, disturbance of hepatic biochemistry with increase of SGOT (68IU/L), SGPT (67IU/L), increase of obstructive ferments with total bilirubin 2mg/dl and indirect bilirubin 1.53mg/dl. The diuresis remained in satisfactory levels 25ml/h up to the 4th day of hospitalization, while the last day it was decreased in 15ml/h. Also there was observed free liquid inside the peritoneum and pleuritic collection bilaterally. The patient after 5 days of hospitalization was transported in a third degree Hospital with thoracic ache and dyspnoea where was finally placed Bullau chest drainage set bilaterally. The syndrome receded in two weeks. The ovaries came back in the physiologic size. There was not achieved a gestation.

Conclusions: The syndrome of hyperexcitation of ovaries constitutes an iatrogenic potentially serious usual (3-23%) problem of facilitated reproduction and methods of excitation of ovaries in infertile couples. The levels of estradiol are themost reliable indicator of prognosis as well as the ultrasound and the laboratorial discoveries. The effect can be decreased with the suitable therapeutic approach.

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Ten weeks prolongation of pregnancy with PPROM: Case report

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32 years old woman with medical history of one dead fetus and two miscarriages, was presented with 21 weeks pregnancy complicated with decreased amniotic fluid index due to PPROM and abdominal pain. Clinical and laboratory tests found: streptococcus B infection, leukocytosis (10 000/µL) and positive C reactive protein. The fetus evolution was monitor by weekly echography and Doppler studies, that constantly relieved single vertical pocket of amniotic fluid of 3.5cm, no malformations and normal fetus growth with a permanent cerebroplacental ratio between normal ranges. The treatment consisted in hospitalize, repose, tocolitic and antibiotics drugs. Antibiotics spectrum was changed every ten days to avoid bacterial resistance. Starting with week 24 the treatment included glucocorticososteroides for acceleration of fetus lung maturation. Delivery labor was in week 31 by caesarean section for fetal benefit. Newborn was a girl, 1700g weight, Apgar score 8 and no necessary respiratory assistance. After 18 months the growth and the neurocomportamental development is still normal.

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Fetal gastro-intestinal obstructions: Spectrum of ultrasound findings and management of newborn

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Objectives: Characterization of ultrasound findings considering fetal gastrointestinal obstruction at different levels and correlation with postnatal evaluation.

Material and Methods:
Analyzes of ten gestations with prenatal findings suggestive of gastro-intestinal obstruction and a case diagnosed postnatal without ultrasound findings.

Results: Ultrasound pictures suggestive of esophageal obstruction (4 cases), found at midtrimester, revealed hidramnios and stomach not visible. Two of these cases went midtrimester fetal deaths, one of them with complex malformations. Fetal autopsy did not confirm esophageal obstructions. Newborn evaluation diagnosed 2 cases of esophageal atresia. Findings suggestive of duodenal obstruction (2 cases) were found at mid and third trimester ultrasound, showing double bubble sign and hidramnios. Postnatal examination revealed one case of duodenal atresia and another of anular pancreas. Intestinal obstructions (3 cases) showed abdominal circumference higher than remaining biometry and distension of gut and colic anses. Two cases were rectal/colonic malformations. The remaining represented a 32nd week pregnancy evaluated at emergency room, with ultrasound evaluation showing gut distension and bradicardic fetus, Resulting in an emergent caesarian section. Newborn had an ileal volvulus. Finally, there was a case without ultrasound findings of intestinal obstruction, representing an imperforated anus. We correlate ultrasound pictures with radiological evaluation of newborn in each case. Newborns were transferred to Pediatric Surgery and submitted to correction of gastrointestinal malformation.

Comments: Prenatal screening policy is an important tool in gastrointestinal obstructions. Fetal ultrasound is of limited value in diagnosing imperforated anus. Although fetal autopsy did not confirm, a previous esophageal obstruction could exist in uterus.

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Prenatally sonographic détection of liver calcifications in a fetus diagnosed at birth 
with a metastatic neuroblastoma

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Background: Neuroblastoma is the most common fetal malignancy. This heterogeneous tumor is derived from sympathetic ganglion precursor cells of neural crest origin. Prenatally diagnosed neuroblastomas generally have an excellent oncologic prognosis.

Case report: A routine sonogram performed at 32 weeks’ on a 39-year-old woman, gravida 6, para 2 revealed an hyperechoic focus measuring less 5mm located in the right liver lobe. Two weeks later, a thorough sonographic survey demonstrated an additional hyperechogenic focus in the left liver lobe without any other abnormalities. A diagnosis of a probable metastatic neuroblastoma was made on the new-born boy based on ultrasound examination and computed tomography (CT) that showed a 2.6cmx1.8cm paravertebral mass infiltrating the celiac axis and two small liver calcifications. At five months of age, a CT-guided core needle biopsy confirmed the diagnosis of metastatic neuroblastoma with no amplified N-myc oncogine. An expectant observation was considered in this unresectable midline retroperitoneal mass that involved major vascular structures; after a short course of close observation, a spontaneous regression was achieved.

Conclusions: When liver calcifications are prenatally detected in a fetus, a thorough sonographic visualization of all the neural crest regions should be carried out with a special attention to renal, suprarenal and paravertebral areas; in addition, motility of the lower extremities would be carefully assessed. Furthermore, fetal magnetic resonance imaging could be performed to rule out an intraspinal extension if a paravertebral neuroblastoma is suspected.

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Fetal anomaly in pregnant women referred to perinatology clinic of Mirza-Kochekkhan hospital

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Aim: Cognition of frequency, variety of fetal anomaly, status of family marriage and termination of pregnancy in these cases is the main aim of this survey.

Methods and Material: We collected data of women who referred to perinatology clinic of Mirza-Kochekkhan Hospital from July 2007 to December 2008. Type of anomaly, involved organs of fetus, gestational age of diagnosis, family marriage and type of it, history of fetal anomaly in family and previous siblings, are collected in questioners and analyzed.

Results: 138 cases studied. Mean age of women were 27.7±5.5. 17.35 percent had multiple anomalies. CNS anomaly was the commonest type and genito-urinary and musculoskeletal systems were others. 44% had familial marriage and first cousin was common type. History of fetal anomaly in other siblings of women was in 10%. Only 61% of anomaly were diagnosed by 20 weeks of pregnancy.

Recommendation: Avoidance of familial marriage may help to reduce of frequency of anomalies and early diagnosis of fetal anomaly can result in better decision of parents to termination or continuation of pregnancy.

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Prenatal diagnosis of a triploidy associated with alobar holoprosencephaly: A case report and review of the literature

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In this case report we present a fetus with an alobar holoprosencephaly diagnosed at 27 weeks and 5 days. Ultrasound examination showed a single ventricle and fused thalami. The interhemispheric fissure, falx cerebri and corpus callosum were not visualized. Associated facial abnormalities included proboscis, and severe hypotelorism. The placenta was large and vacuolated. Prenatal karyotyping revealed 69 XXY.

After consultation patient opted for termination of pregnancy. Neonatal examination confirmed sonographic findings.

We present a late presentation of a case of holoprosencephaly associated with triploidy and a review of the literature.

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Postnatal management in infant in whom the diagnosis of ileal atresia was established during prenatal period

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Objective: To assess the prenatal diagnosis, perinatal outcome and postnatal outcome in fetus in whom the diagnosis of ileal atresia was established.

Methods: Maternal age, indication for sonography, gestational age at diagnosis, other sonographic abnormalities, perinatal, postnatal care, operative treatment and postoperative follow up were noted.

Results: A 34-year old primigravia was referred to our Department in 34th week of gestation for ultrasonographic evaluation. Previous scans were qualified as normal for given gestational age. Dilatation of the fetal ileum and stomach was detected and the presence of mild polyhydramnion. No other fetal anomalies were seen. Fetal karyotype was normal male. Diagnosis of the atresia of fetal ileum was established. At 40th week of gestation a 3590g male baby was delivered and admitted to the Clinic of pediatric surgery. Clinical, ultrasonographic, radiologic examinations were done. Distension of the abdomen, vomiting and melena were major clinical signs. Surgical treatment was carried out. Histopathological diagnosis was: haemangioendothelioma kaposiforme mesenterii.

Discussion: Congenital haemangioendothelioma kaposiforme mesenterii is a rear disease. The most common localization of the kaposiform haemangiomas are skin, retroperitoneum, liver and lungs. This disease if often associated with Kasabach-Merritt syndrome. In our case this syndrome was not present.

Conclusion: In case of a suspicion of prenatal ileal atresia, the prenatal detection and search for possible associated fetal anomalies is of great importance for the determination of the further course of pregnancy. Prenatally and postnatally close prenatal consultation of the neonatal surgeon will favorably influence the perinatal outcome.

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Premature constriction of fetal ductus arteriosus after maternal assumption of acetaminophen (paracetamol): Report of two cases. Idiopathic or drug induced?

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Intrauterine closure of the ductus arteriosus (DA) is a rare but dangerous complication of term pregnancy. It can be idiopathic or secondary to non steroidal anti-inflammatory drugs (NSAID), through their PGE syntetase inhibitor action. Acetaminophen (ACAP) is commonly used in pregnancy for pain medication and considered harmless for the fetus. However its mechanism of action is incompletely understood. ACAP is believed to act selectively in the brain, but showed activity in constricting fetal DA in animal models. However it has never been reported as possible single agent constricting human fetal DA. We report two cases of restrictive ductus: both patients reported only ACAP assumption. In the first case the mother had taken NSAIDs for the whole duration of pregnancy due to skeletal-muscle pain, but reported only high dose ACAP assumption in the last weeks. She presented at 39 weeks with acute fetal right heart decompensation, oligohydramnion and fetal distress. Echocardiographic diagnosis of ductal closure indicated immediate caesarean delivery. The other case was referred to fetal echocardiography for unexplained right heart dilatation, and showed DA restriction but no cardiac decompensation. Labor induction and vaginal delivery were possible. The mother reported only assumption of acetaminophen in the last days. Both cases had a favorable neonatal outcome. The Authors recommend caution in prescription of any drug in the last weeks of pregnancy and close echocardiographic assessment of ductus patency if NSAIDs are used. Further studies on acetaminophen mechanism of action are warranted to clarify its involvement in this potentially lethal complication.

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Congenital pulmonary alveolar proteinosis – A case report

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Introduction: Pulmonary alveolar proteinosis is a rare entity with two known forms, congenital (CPAP) and acquired. Congenital form is manifested in first few hours of life as severe respiratory failure with fatal outcome with accumulation of PAS positive protein in alveoli. Possible causes are surfactant protein B deficiency or GM colony stimulating factor receptor changes.

Case Report: female newborn from third pregnancy, normal delivery at 38 GW, BW 3,150g, BL 54cm, head circumference 34, AS 6/7. Cyanosis after birth, with slight improvement after oxygenotherapy. Pulmonary auscultatory findings: rales. First child from same family healthy, second child born at 28 GW died after three weeks, with diagnosed respiratory distress syndrome. On admission: intubated, ventilated during transport, cardiac arrest twice during transport. Few agonal breaths present, pale skin, cyanosis, pulmonary auscultatory findings: bronchial breaths. HR: 20-40/per minute. Chest X ray: «ground glass» appearance with air bronchograms. Echocardiography: extremely poor contractile heart function, almost absence of mechanical heart activity, patent foramen ovale, there is no structural cardiac anomalies. Treated with IPPV mechanical ventilation (PIP 39 mbar, PEEP 8 mbar, 60 breaths/ per minute, FiO2=0.9), continuous intravenous infusion of Epinephrine and Dopamin, intravenous fluids (glucosae 10%), heart chest compressions. CPR duration - 1 hour. Lethal outcome after seven hours of life. Autopsy: partial fetal atelectasis, alveolus filled with thick eosinophilic content, cell detritus, lipid vacuolas and eosinophiles. PAS (periodic acid schiff) positive hyaline membranes and alveolar content.

In conclusion: cause of death was fatal congenital pulmonary alveolar proteinosis.

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Convulsions in pregnancy – what can it be? A clinical case review

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Introduction: In the peripartum period the most frequent cause of convulsions (first time diagnosed) is eclampsia. This is a potentially fatal clinical condition that must be properly diagnosed and treated. But when we have focal neurologic deficits, prolonged coma or atypical eclampsia, we should make differential diagnosis with other causes such as stroke, occupying lesions of the brain, metabolic disorders, idiopathic epilepsy, etc.

Clinical case: Woman 27 years old, gipsy ethnicity, IIIGIIP, 32 weeks and 4days of gestational age, no prior health problems known, including in the first two pregnancies, with gestational hypertension diagnosed at 28 weeks and treated with methylidopa 250mg 3 times/day. Arrives at the hospital with seizures, BP 192/106mmHg, oliguria and generalized edemas. A caesarean is performed after stabilizing vital parameters and stopping of the seizures. After birth, the puerpera varied between agitated mental state and confusion, BP became stable using labetalol and seizures were prevented with magnesium sulfate. Despite the tensional normalization, the puerpera never recovered total awareness and a CE-MRI and an EEG were performed detecting severe hydrocephaly and an occupying lesion of the cerebellum. A ventricle-peritoneal derivation was performed and CE-CT scan, angiography and other tests were performed to discover the underlying cause.

Discussion and conclusion: Despite the prevalence of eclampsia in a pregnant woman with seizures, we should always suspect and study other potential causes when the normal resolution doesn’t occur in spite of proper treatment.

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The limits of genetic diagnosis. A case series

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Aims. The authors emphasize the genetic diagnosis limits in 3 pediatric cases characterized by perinatal morphological abnormalities.

Methods: The authors present 3 infants with growth impairment, psycho-motor skills delay and congenital anomalies. These cases were further evaluated during early infancy. First case: 6 month-old girl with elfin face, long philtrum, low inserted ears, legs edema. The investigations have excluded skeletal dysplasia, the endocrine and storage diseases. Second case: 2 month-old male with microcephaly, cleft palate, hypotelorism, recurrent seizures; the investigations have revealed holoprosencephaly and cardiac malformation. Third case: 4 month-old boy with cyanosis, ear shape anomaly, unilateral radius aplasia, homolateral first metacarp and thumb aplasia; the investigations have confirmed the cardiac malformation. The authors have focused on the radius agenesis syndromes.

Results: First case: the karyotype has revealed 46 XX del (X) (q26; qter). It’s difficult to establish the link between terminal Xq deletion and facial dimorphism. The patient will be followed up regarding the “premature ovarian syndrome” possibility at adolescence. Second case: the karyotype was normal (46, XY); the authors consider the utility of CGH-array to identify gene anomalies known to be associated with holoprosencephaly (ZIC2, SIX3, TGIF, SHH). Third case: „Multiplex ligand dependent probe amplification” analysis didn’t identify exons abnormalities for TBX5 and SALL4 genes. Even normal genetic tests, the authors can’t exclude Holt-Oram and Okihiro syndromes.

Conclusions: All infants have had postnatal morphological anomalies justifying genetic evaluation. Among infants, the karyotyping was first evaluation for 2 of them. For diagnosis accuracy, all cases need further cytogenetic tests.

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Prediction of birth weight by measurement of body circumferences in sudanese newborns

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In Africa scales to measure birth weight are often not available. The aim of this study was to develop a simple formula to predict birth weight by body circumferences which can be measured easily by an inelastic tape. Methods: Anthropometric measurements were taken within 24 hours of birth from a 1,000 mothers and their singleton infants. Gestational age ranged between 28-42 weeks and birth weight between 800-5,100g. Data were analyzed by multiple regression with backward selection. Results: A simple formula using chest (CC), mid thigh (MT), and head circumferences (HC) was obtained to predict BW as follows: \( BW(g) = 96.8 \times CC + 74.4 \times MT + 84.5 \times HC - 3960 \) with a standard error of 285g. For birth weights <2000g, specificity is near 100% and the sensitivity is >80%. Applying a cut off point of 2500g, all infants (100%) with birth weight <2000g are correctly identified. Conclusion: Our formula will enable the health worker in developing countries to select appropriate low birth weight babies for referral to an equipped health facility. To which extent can our model be adapted to fetal weight measurement is open to question, and we invite perinatologists to investigate this matter.

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Preeclampsia-clinical and ultrasound parameters in assessment of fetal well being

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Preeclampsia is a great risk for mother and fetus during pregnancy. We wanted to evaluate clinical, laboratory and ultrasound parameters in assessment of fetal well being in pregnancies with preeclampsia and gestational hypertension. Our study included two randomized groups of 28 patients each. More than 90% of our patients were between 20 and 35 years of age. Three quarters of them was in their first pregnancy. Family history of hypertension was positive in 25% of cases. Only 4% of pregnancies were terminated before 32 week of gestation. The way of termination was operative in 66% of cases. Fetus from pregnancies with preeclampsia was less than 2000g in 14%, and APGAR score was less than 3 in 9% of patients. Pathological Doppler flow in fetal circulation was registered in 13 patients. Fetal asphyxia was detected by CTG and Doppler assessment in 13 patients, but APGAR score less than 7 had 5 newborns. Using all available diagnostic tools in predicting of fetal outcome in patients with hypertension and preeclampsia can lead us to false positive Results in even 60% of cases.

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**Do macromorphological features of the human placenta influence somatic and psychomotor development of the newborn and early infant? A historic question revisited.**

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Objective: We examined the meaning of placental weight, form (massive and thick or extended and flat) and circumference for early somatic and psychomotor childhood development.

Methods: In this prospective study fresh placentas (N=265) were measured for weight and circumference and correlated with neonatal data. A subset of placentas statistically defined as ‘massive’ (circumference <10th percentile) and ‘extended’ (circumference >90th percentile) was correlated with somatic and basic psychomotor parameters during the first four years of life. A ‘medium’ category (circumference 45th-55th percentile) served as control.

Results: Placental weight correlated with birth weight (r=0.53, p<0.0005) and mean infantile weight until month 48 (r=0.29, p=0.016). Placental circumference weakly correlated with birth weight (r=0.17, p=0.011) but not with mean infantile weight. A better correlation was found between birth weight and infantile weight (r=0.47, p<0.001). Placental extremes (massive, medium, extended) demonstrated significant influences only on very early somatic growth (day 1 to month 4): Massive placentas were associated with heavier and taller children (p=0.02 – 0.033). Markers of early psychomotor development (first sitting, crawling, running, one- and two-word sentences) were not related with placental weight or circumference nor with extremes of placental morphology.

Conclusion: Placental weight and circumference seem to influence very early somatic growth until 4 months of life but not psychomotor development.

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In utero 3D visualization of normal and abnormal fetal brain development

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Purpose: This in vivo and in utero MR study aimed to 3D visualize cerebral fiber pathways in normal and pathological conditions.

Methods: An axial single-shot echo planar diffusion tensor (DT) sequence (32 non-collinear diffusion encoding directions, reconstructed voxel size 1.44/1.45/4.5mm) was acquired in 40 unsedated fetuses without signs of cerebral pathology (mean 28.2 gestational weeks – GW) using a 1.5 Tesla MR scanner. This group was compared to 21 fetuses with brain abnormalities (complex malformations 7, ventriculomegaly 6, brain edema 3, callosal agenesis 2, ischemic lesions 3). Using the Philips registration package a multiple region of interest analysis was performed in order to 3D visualize the sensorimotor, the callosal and the frontopontine connectivity of the fetal brain.

Results: 3D visualization of all major fiber trajectories of the fetal brain in utero was possible in over 40% of cases. Fiber bundles travelling through the posterior limb of the internal capsule were depicted as early as 18 GW. The normal appearance of the callosal genu and splenium could be readily compared to the aberrant Bundle of Probst in a case of callosal agenesis. Intermingling of genu and frontopontine trajectories represented the histologically described periventricular "crossroads". Severe fetal brain edema did not impair the visualization of trajectories, but measured apparent diffusion coefficients values were significantly reduced compared to age matched controls.

Conclusion: DTI allows to visualize the 3D fiber architecture of the developing fetal matter in vivo and in utero and has the potential to detect and characterize abnormal microstructure of the fetal brain.

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Morphology of cerebral ischemic infarcts in newborns

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Aim: Investigation of the frequency and morphologic picture of cerebral ischemic infarcts in newborns with perinatal pathology.

Materials and methods. We made a morphological research of the brain by the method of impregnation by Homory at 105 newborns with acute (27), chronic hypoxia (36), infectious pathology (42).

Results: Histological we revealed a destructive changes of nerve cells of varying degrees of expression from hromatolizis to lipid dystrophy and vacuolation; disorders of haemocirculation in form of plethora of arterial and venous vascular ways of all sizes; in 59.5% of cases was stasis, sludge in paretic advanced vessels, a formation of single or multiple erythrocyte, platelet and fibrinous clots; in 35% cases not founding of bloodstream; in 38.1% revealed diapedetic hemorrhage in the connective tissue, and in the walls of vessels, stroma and vascular plexuses. Structural changes of vascular were characterized as: fibrotic changes in the walls at 40.7% of infants, loosening of argyrophilic frame at 31.0%, breaking of fiber of vessel walls at 16.5%. The end of hemocirculatory disorders in the brain has been the reduction and / or cessation of cerebral circulation and the development of cerebral infarcts.

The focuses of necrosis are localized in the cortex, white matter, periventricular area and were at varying stages of their development (from necrosis to gliosis), what testify that they appear non-simultaneously.

Thus, we established a high frequency of cerebral ischemic stroke in newborns, development of which is based on neurodystrophical and circulatory damages.

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Metabolism and fetal body surface – Quantification of the subcutaneous fat layer with MRI in normally and abnormally developed fetuses

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Aim: To assess the age-dependent fetal subcutaneous fat layer (SCFL) of normally developed fetuses with MRI. Ongoing studies to evaluate disturbances of development of the SCFL include hormone imbalances such as hypothyroidism, diabetic pregnancies and other metabolic diseases as well as intrauterine growth restriction (IUGR).

Methods: 115 MRI examinations of normally developed fetuses, performed on 1.5T (Philips) at gestational week (GW) 28 to GW 39, were evaluated retrospectively. The fetal SCFL was measured in mm at the upper arm, upper and lower back, above the umbilical cord insertion, at the hip and the thigh using T1-weighted images in sagittal and axial planes. Data were compared to SCFL measurements of fetuses with underlying (maternal) disease.

Results: Measurements in normally developed fetuses ranged from a minimum of 2mm at GW 28 at all measured points, up to 4mm at the trunk and 6.5mm at the extremities at GW 39. The measurements showed high consistency and allow the establishment of a standard of reference to determine the developmental status in fetuses. Increased thickness of SCFL was recognized in fetuses with maternal hypothyroidism, diabetic pregnancies and fetal metabolic diseases; decreased thickness was found in IUGR fetuses.

Conclusion: The SCFL of normally developed fetuses is easily detectable from GW28 in T1-w images, and increases depending on the gestational age. These data provide physiological benchmarks to evaluate fetal size and developmental status. Based on these normal ranges abnormalities of the thickness of the SCFL can be recognized enabling to imply on the underlying disease.

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Truncus arteriosus tip 1 with antenatal diagnosis

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Truncus Arteriosus complicates approximately 0.01/1000 live births. In this case report we discussed Truncus Arteriosus Tip 1 case detected in utero with echocardiographic findings. A 31 year old pregnant woman at 26 weeks of gestation referred to our clinic. She hasn’t got a consenginous history. According to the fetal echocardiographic findings we diagnosed Truncus Arteriosus Tip 1. The big part of the congenital heart diseases occurs in pregnancies with no risk factors. If we visualized the subaortic ventricular septal defect in the fetal heart, we can detected the associated abnormalities; such as Truncus Arteriosus.

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Three cases of placental fetal thrombotic vasculopathy with varied clinical courses

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Fetal thrombotic vasculopathy (FTV) in the placenta is characterized by thrombosis of the placenta and villous changes along the periphery of the thrombotic lesion. FTV results in hypoxia and ischemia due to placental dysfunction and can adversely affect the fetus or neonate. We report 3 cases of placental FTV with varied clinical courses. Cases 1 and 2 (GA 36w 5d) are those of monochorionic diamniotic twins with a history of treatment for threatened premature delivery in the fetal stage. The first twin (BW 2,930g) was born with severe asphyxia and died 5 hours after birth. The other twin (BW 3,024g) was born with mild asphyxia and needed treatment with nasal continuous positive airway pressure. In case 3, the patient (GA 27w 4d; BW 746g) had a history of oligohydramnios and heart failure in the fetal stage; showed elevated transaminase levels, coagulopathy, and hypoglycemia at birth; and was diagnosed with trisomy 21 after birth on the basis of pathognomonic findings. In all cases, FTV was diagnosed by pathological examination. It is very difficult to prenatally diagnose FTV or accurately predict its adverse effects in the fetal stage because the direct etiology of FTV remained unclear. Moreover, it is difficult to diagnose FTV on the basis of its progression pattern during the early postnatal period because the condition can have various clinical courses. Therefore, pathological examination of the placenta should be conducted in the case of neonates with symptoms of coagulopathy, liver dysfunction, or birth asphyxia with an unknown etiology.

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Growth factors orchestrate cell growth, differentiation and proliferation during embryogenesis. The aim of our study was to establish the appearance of some growth factors and their receptors in tissues affected by tubal pregnancy. The immunohistochemical distribution of TGF beta 1, bFGF, FGFR, NGF, NGFRp75, IGF-1, IGF-1R has been identified. The distribution of these factors was detected semiquantitatively. Moderate number of FGFR and NGF containing structures were seen in each slide. NGFRp75 was observed focally only in nerve fibers. IGF-1 was widely distributed in fallopian tube epithelium but IGF-1R focally stained apical surfaces of tubal epitheliocytes. Despite epithelium IGR-1R stained only mesothelium and was absent in chorionic structures. Cytotrophoblast and sincytiotrophoblast moderately contained FGFR and IGF-1. FGFR stained all extraembryonic mesenchymal cells, when IGF-1 only single of them. Sincytiotrophoblast and extraembryonic mesenchyma showed NGF immunoreactivity. Peripheral trophoblast focally contained FGFR, bFGF, NGF and IGF-1 positive cells. IGF-1 and bFGF as well stained macrophages and neutrophils. TGF beta 1 negative reaction was typical for all the tissues in any case of tubal pregnancy we analyzed. Conclusions: TGF beta 1 is absent both in mother and conceptus tissues; fallopian tube tissues express more FGFR than bFGF and testify the stimulation of compensatory adaptation of the organ; the presence of NGF in structures of fallopian tube with absence of NGFRp75 indicates the failure of cell interaction; the deficit of IGF-1 and the absence of IGF-1R are suggested to be a Result gestation's growth restriction and impaired process of trophoblast invasion.

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Cyto-chemical markers in placenta at the time of delivery, indicating risk factors for increased apoptotic cell death

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Introduction: Placental tissues produce cytokines, believed to modulate immune system for successful pregnancy. Pathological pathways of mismatch of those mechanisms have not yet been completely elucidated. Hypoxia leads to apoptosis in placenta (Hung), induced stress may regulate production of placental TNFα (Tai-Ho Hung). Intermittent oxidative stress in labor leads to increased TNFα in placental tissues (Tereza Cindrova-Davies). Aim. To compare cyto-chemical markers of apoptosis in placenta.

Materials and methods: 15 placentas: 4 pre-term and 11 term. Risk factors were identified by antenatal history and questionnaire. Specimen was examined by antibodies: TNFα rabbit polyclonal, abcam, 1: 100; TGFβ mouse monoclonal, abcam, 1: 1000; Terminal dUTP nick end labeling (TUNEL), ROCHE, 1: 10. Evaluation semiquantitatively: from 0 (no positive structures in visual field) to ++++ (abundance).

Results: Abundance of TGFβ was observed in the pre-term placenta with the higher risk for infections and strong structure degeneration; occasional or few structures were found in the others. The same placenta showed abundance of TNFα; expression in the other samples varied from no one to moderate. TUNEL revealed numerous structures of apoptosis in two pre-term placentas; more structures were in term placentas from vaginal deliveries than in placentas from elective Cesarean Sections. Signs of apoptosis were significant in a case of adverse outcome of term delivery due to fetal distress in a low risk pregnancy patient. Conclusions. Markers for destructive changes in placenta TGFβ, TNFα and apoptosis can indicate processes having impact on outcome in comparable clinical situations.

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Intrauterine death in multiple gestation: Implications for surviving twin

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The incidence of multiple gestation has increased as a Result of the increase of the fertility enhancement therapy. Early fetal loss is more common than clinically recognized.

Male infant born at term had congenital aplasia cutis and multiples fractures, a monochorionic and diamniotic placenta and a 6cm intrauterine lithopedion.

Female preterm infant born at 35 weeks of trigeminal pregnancy, with microcephaly and sutured bones. Follow-up: cerebral emiatrophy with cerebral palsy and death at 5 months. The second born developed a moderate developmental delay at 1 year. The third fetus died at 22 wks, papyraceus. Morphological evaluation revealed a trichorionic and triamniotic placenta.

A female infant, delivered by CS by fetus maceratus at the 7th month, had a sacrococcygeal teratoma. She had a normal neurological development after surgery. Morphological evaluation revealed a monochorionic and monoamniotic placenta.

In monochorionic twins, the death of one twin has adverse effect on the surviving fetus. As one fetus dies, the living twin may exsanguinate into the dead monochorionic twin through vascular anastomosis, causing an hypoxic episode. In dichorionic twins, complications to the surviving co-twin are more unusual. Disruptions of the central nervous system are the most common complication (72%), followed by the gastrointestinal system (19%), kidneys (15%), lungs (8%), cardiac malformations and aplasia cutis.

Twin dead syndrome is a rare condition with intrauterine death and anomalies in the surviving twin. Like-sex twins are at greater risk of cerebral palsy, probably for twin-twin transfusion problems associated with monochorionicity.

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The diagnosis difficulties in a case with macrocephaly

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Background and aims. Alexander Disease is an extremely rare and progressive neurological disorder characterized by white matter degeneration. The authors emphasize the diagnosis difficulties in a case with macrocephaly (+3SD) discovered during neo-natal period. Methods. The authors present a girl that was followed up in the context of higher head circumference identified early after birth. She was often admitted for parenteral nutrition because of swallowing difficulties. Personal history: normal development from physical and neurological points of view up to 2 years of age when she had first seizures episode; during the last 5 years she has presented progressive head enlargement, the second episode of seizures (7 years of age), failure to thrive. Among clinical features: macrocephaly, psychomotor retardation, increased muscle stiffness and spasticity, behavioral skills regression, growth failure. Results. The investigations revealed normal values for: urinary organic acids, long chain fatty acids, arylsulfatase A, galactocerebrosidase, beta-galactosidase, beta-hexosaminidase. MRI exam has diagnosed a hydrocephaly with cerebral white matter abnormalities and the emission protons spectroscopy has shown low level for N-acetyl aspartate and increased values for myo-inositol. The authors have excluded the leucoencephalopathies without macrocephaly. Among leucoencephalopathies with macrocephaly, the authors have excluded der Knapp leucodistrophy and Canavan’s disease. The genetic analysis has identified a mutation of GFAP gene (chromosome 17, exon4: c715 p. R. 239 C). Consequently, the authors has established Alexander disease diagnosis. Conclusion. The Alexander disease diagnosis depends on genetical evaluation. The authors propose a diagnosis algorithm for leucoencephalopathies based on clinical features, MRI criteria, laboratory and genetic investigations.

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Cleidocranial dysplasia with severe calvarial phenotype in a patient with a new RUNX2 mutation

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Cleidocranial dysplasia (CCD, MIM 119600) is a skeletal dysplasia characterized by delayed closure of the skull sutures, wide-open fontanelles, mild face hypoplasia, hypoplastic or aplastic clavicles, and dental anomalies. Mutations in the RUNX2 gene cause CCD, however until now no clear genotype-phenotype correlation has been described.

We report a baby girl with CCD and severe dysplasia of the skull bones. At birth, there was softness of the skull with normal scalp and skin. Cranial X-ray showed hypoplastic parietal and frontal- but normal facial bones. CT and MRI showed normal intracranial structures without ventricular dilation. Calcium, phosphorus and alkaline phosphatase were normal. Renal ultrasound identified normal kidneys. Full skeletal survey showed hypoplastic clavicles. Skull X-rays showed spontaneous but incomplete bone growth. She presented a normal physical and psychomotor development, with progressive macrocephaly.

RUNX2 gene molecular test identified a p.Val124Serfs mutation in heterozygosity form in exon 1. This deletion of seven nucleotides leads to a frameshift and a premature stop codon. This mutation has not been described in the literature yet. Testing of the parents didn’t identify the mutation. It most probably arose as the Result of a new mutation.

Until now 91 different mutations in the RUNX2 gene have been described, from which 22 are small deletions. The atypical presentation in this case with severe calvarial phenotype point out the phenotypic variability associated with mutations in the RUNX2 gene and suggest the role of additional factors in the development of the disease.

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Management of a complete congenital sternal cleft: Case report

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Introduction:
Partial or complete sternal cleft is a rare congenital anomaly in which the heart, extremely rare with severe anomalies, is orthotopically located and covered with an intact pericardium and skin.

Case report:
We report a case of complete sternal cleft without associated cardiac defects or other anomalies. A 2440-g female neonate, born at 36Wks of normal delivery, Apgar 5, presented a complete cleft sternum which was recognized antenatal. The sternum was completely bifid with an inter-ridge distance of 5.5cm, through which the heart and cardiac pulsations are prominent. Initial management included mechanical ventilation, systemic antibiotherapy and echocardiography which showed no cardiac abnormalities. Surgical repair of the chest wall defect was performed after 3 weeks. The gap was primary closed up by drawing near and “X” suture of the sternal ridges followed by a complete closure of muscles and skin. The patient was discharged after 1 month post surgery with a stable cardio-respiratory function and weight gain of 500g.

Conclusions:
Advances in fetal ultrasound techniques are very utile in the early recognition of the congenital thoracic wall deformities. Surgical repair for sternal clefts is recommended in infancy within the first 3 months of life when the chest wall is most flexible and primary closure is accomplished without difficulty. The successful repair of such anomalies is dictated by the presence and the severity of the cardiac anomalies rather than the type of surgical approach itself.

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A newborn with sirenomelia: extreme form of caudal regression syndrome

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Objective: Sirenomelia is an extreme form of the caudal regression sequence. The prevalence has been estimated at about 1 in 100,000 births. Malformations include a single lower limb, urogenital anomalies, imperforate anus and sacro-coccygeal agenesis. We report a case with sirenomelia which has also known as Type V caudal regression syndrome and reviewed the etiology.

Case report: A 6-hours-old infant was referred to our NICU with multipl congenital anomalies. The infant was born at 38 weeks gestational age to a 29 year old mother who had twin pregnancy. Other infant was normal. On physical examination vital signs were within normal limits. There is a hypoplastic single lower limb. External genitalia and anal orifice were not developed, myelomeningocele, omphalocele were other associated findings. Ultrasonography showed unilateral agenesis at the right side and cystic structure of the left kidney and absence of the bladder. The infant survived for twelve days, the parents did not approved any surgical intervention. Autopsy was performed.

Conclusion: Sirenomelia in twin pregnancies was reported previously in which only one infant was affected similar to our case. Although etiological heterogeneity is present, it is not thought to be a hereditary condition.

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Intrauterine constraints causing tissue tensions in the newborn, related to symptoms and alleviated via manipulation

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Space constraints in utero translate into tissue tension and asymmetries of the dura mater, ligaments, cartilage, muscle and tendon which, then, cause asymmetry in growth of bone. Asymmetry in all these tissues cause symptoms in the newborn, infant and toddler and can interfere with optimal neurologic growth and development of the child. Symptoms can persist and/or change during the lifespan of the individual and include not only physical but mental and emotional disturbances. Manipulation of these same tissues in the mother during pregnancy has been shown in hands-on practice to prevent distortions in the newborn as well as ease pain of pregnancy and childbirth. Manipulation of the newborn, infant and toddler has been shown to alleviate many common symptoms of the perinatal period and beyond.

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Comparison of oral and vaginal misoprostol for cervical ripening before evacuation of first trimester missed miscarriage

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Objective: assess the effectiveness of Misoprostol in cervical ripening before evacuation of conceptional products in 1st trimester missed miscarriages, and compare between 2 routes of administration (oral or vaginal).

Patients and Methods: this randomized controlled study was carried out in Baghdad Teaching Hospital in 2006. 120 women with first trimester missed miscarriages were divided into 4 groups 2 study groups were randomized for oral and vaginal (400 mcg) misoprostol priming of cervix and 2 control groups were randomized for oral and vaginal placebo. All underwent surgical evacuation of conceptional products after 3 hours.

Measured outcomes were: post medication cervical dilatation (PMCD), time needed to dilate the cervix surgically, blood loss and development of side effects of misoprostol.

Results: PMCD was higher in the Misoprostol group (7.07±1.36mm for oral Misoprostol, 7.77±1.22mm for vaginal Misoprostol) versus the control groups (2.43±0.5mm).

PMCD was significantly higher in the vaginal misoprostol group compared to the oral group (p=0.04)

The time required to dilate the cervix in the Misoprostol group was shorter compared with placebo (oral Misoprostol 1.91±1min, vaginal Misoprostol 1.7±0.8mm vs. 4.76±1.6min for oral placebo, 5.13±1.4min for vaginal placebo).

There were no significant differences in the amount of blood loss between oral and vaginal misoprostol groups (p=0.74, p=0.62), and gastrointestinal side effects were significantly more in the oral Misoprostol group(p<0.001).

Conclusion: Misoprostol is an effective cervical priming agent when administered either orally or vaginally before evacuation of conceptional products in termination of 1st trimester missed miscarriage.

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Heterotopic pregnancy with Tweens in Utero

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Heterotopic pregnancy is very rare condition in spontaneous pregnancy, it is more frequently after methods of assisted reproduction. We present case report of Tweens in Utero and one gestational sac in left fallopian tube after ICSI/ET. Patient was 31 years old and first time came in our institution in 12th week of gestation. She had signs of hemorrhagic shock. Ten weeks before she undergo ICSI/ET procedure with transfer three embryos in utero. Level of beta hCG 14 days after procedure was 288 mUI/ml. First US examination in regional hospital show trigemini in utero. Transvaginal scan in our institution demonstrated Tweens in utero CRL 38mm and 39mm, both with negative heart rate, and massive fluid in abdomen cavity. She was operated and we found rupture of left fallopian tube with pregnancy. Pathohistological examination confirm diagnosis. Heterotopic pregnancy is more frequently after methods of assisted reproduction especially after transfer more than two embryos in utero. It is very important to think on this rare condition and with early diagnosis prevent tube rupture and give chance to continue pregnancy.

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Prenatal exposure to threatened miscarriage and adult cognitive function

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Background: Threatened miscarriage (TM) is a common pregnancy complication. Little data exist on long-term cognitive function after prenatal exposure to TM. We examined this association among Danish draftees.

Methods: We conducted a prevalence study in a northern Danish conscription district among men born as singletons in 1978-1983 and presenting for the mandatory army evaluation, which includes intelligence testing. These data were linked with the conscripts’ birth data from the Medical Birth Registry. Maternal TM was ascertained from the National Registry of Patients.

Results: Results of intelligence testing were available for 13767/15625 (88%) of the eligible men. The remaining 12% were granted a-priori health-based exemption. The overall prevalence of TM exposure before 23rd gestational week was 3.6%, and it was higher among men with the health-based exemption than among men without (5.0% vs. 3.5%). Greater prevalence of TM was associated with maternal age >35 years (5.0%); maternal history of diabetes (6.8%); preterm delivery (9.3%); and caesarean delivery (5.8%). 2053 of the 13767 men with intelligence-testing data (14.9%) had a low (<85) IQ score. The prevalence of low IQ was 16.8% among the exposed to TM and 14.8% among the unexposed. Prevalence ratio was 1.13 [95% CI: 0.93-1.39] after adjusting for maternal marital status, age, parity, diabetes, preterm birth and growth restriction. TM exposure was associated with a mean change in IQ of -1.1 points [95% CI: -2.5; 0.2] after adjustment for covariates.

Conclusion: There was little evidence for the association between prenatal exposure to TM and adult cognitive function.

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Heterotopic pregnancy – acute abdominal pain in a 10 week pregnancy

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Heterotopic pregnancy is the co-existence of intrauterine and ectopic pregnancy. It was first described by Duverney in 1708 and it is still a potentially life threatening event. Although common with assisted reproductive techniques, naturally occurring heterotopic pregnancy is rare. Its incidence has been reported as 1/8000-1/30000.

The authors report the case of a 27-year old gravid 2, para 1 woman with a previous caesarean section. She presented with amenorrhea of 10 weeks and acute pelvic pain. The ultrasound study showed a live intrauterine gestation and a considerable amount of free abdominal fluid. Diagnostic laparoscopy revealed ruptured tubal pregnancy and left salpingectomy was performed. Postoperatively, her course was uneventful with discharge on the third day. After premature rupture of membranes at 35 weeks of gestation a healthy preterm newborn was delivered without complications.

Heterotopic pregnancy, though rare, can still Result from natural conception. A high index of suspicion should be raised in instances of acute pelvic pain in the face of a documented intrauterine pregnancy. Heterotopic pregnancy is associated with very high maternal morbidity and fetal loss. Nevertheless, a timely intervention can Result in a successful outcome and the survival of the intrauterine fetus is feasible. With early diagnosis and treatment, the chance of intrauterine pregnancy to continue normally increases up to 70%.

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Ectopic pregnancy in previous caesarean scar: A case report

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Background: Ectopic pregnancy in a previous caesarean scar occurs in about 1 in 2000 pregnancies and accounts for 6 percent of ectopic pregnancies among women with a prior caesarean delivery. It has potentially devasting complications such as uterine rupture and bladder invasion.

CASE: We describe the case of a 40 year old woman G3 C2 who came into our hospital with the diagnosis of possible pregnancy in a caesarean scar. She had no symptoms by that time. The transvaginal ultrasounds (US) showed a gestational sac with an embryo, CCL of 15mm with cardiac activity on the right side of a CS scar in the width of miometrium, 5mm from the bladder. We performed a total abdominal hysterectomy, confirming the US diagnosis and solving the problem. We present iconography from ultrasounds and surgery.

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Successful medical treatment of a caesarean scar ectopic pregnancy: a case report

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Introduction: Pregnancy in a previous caesarean scar is one of the rarest forms of ectopic pregnancy. Different treatments have been reported, however because of its rarity, no standard management has been defined. A case of caesarean scar pregnancy successfully treated with methotrexate is presented.

Case Report: A 32-year-old woman gravida 2, para 1, with a previous caesarean section 2 years before, underwent a transvaginal ultrasound at 9 weeks of amenorrhrea in a routine appointment. It revealed a 30x25mm gestational sac with an embryo without cardiac activity and a CRL equivalent to 7 weeks in the anterior part of the uterine isthmus, at the level of the caesarean scar, bulging beyond the anterior contour of the uterus (total mass size, including trophoblast: 54x42mm). The uterine cavity and the cervical canal were empty. The serum $\beta$-HCG concentration was 23,325,80 mUI/mL. There were no symptoms or vaginal bleeding. Intramuscular methotrexate was administered in dose of 50mg/m2. Three days later $\beta$-HCG level was 24,886,15 mUI/mL and in the following day a second dose of methotrexate (50mg/m2) was administered. Thereafter $\beta$-HCG levels started to drop. She remained asymptomatic and only had vaginal staining after the second dose. The patient was discharged 12 days after admission. $\beta$-HCG become negative 67 days after the first methotrexate dose. A transvaginal scan performed one year later showed only a well-defined nodular image with 13x8mm without vascularization in the caesarean scar.

Discussion: Methotrexate may be a valuable conservative management option of caesarean scar pregnancy.

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Uterine artery embolization (UAE) for cervical ectopic pregnancy: The choose of a technique for preservation of fertility

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Cervical pregnancy is an uncommon ectopic pregnancy that accounts for approximately <1% of all extrauterine gestations. This rare condition has been associated with a high morbidity and, in the past, frequently leaded to hysterectomy as a life-saving procedures with loss of fertility of the patients affected. Early diagnosis has improved with the use of transvaginal ultrasonography and the execution of a pelvic Magnetic Resonance. A conservative treatment by preoperative bilateral angiographic uterine artery embolization (UAE) combined with curettage is today a valid and consolidate approach because will control the blood flow, preventing severe hemorrhage, and will preserve the fertility.

We describe our experience with a patient conceived spontaneously 2 years after the UAE followed by immediate evacuation of a cervical ectopic pregnancy. Conservative management was planned because the patient wanted to preserve her fertility. The patient resumed menstruation 35 days after embolization, although her menses were irregular for six months. The pregnancy was uneventful until the 36th weeks of gestation. The patient was undergone to caesarean delivery for metrorrhagia and placenta previa. A 2,320g male fetus was delivered, with Apgar scores of 5 and 8 at 1 and 5 minutes, respectively.

This case suggests that using preadjuvant UAE may be an useful approach for the treatment of cervical pregnancy in patients who desire children in the future even if major obstetrical complication may occur.

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Laporoscopic Milking for a Heterotopic Pregnancy: A Case Report

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Introduction: Ectopic pregnancy (EP) refers to implantation of a viable zygote outside the uterine corpus. Heterotopic pregnancy (HP) is the simultaneous of two or more implantation sites and believed to be about 1/4000 in the general population. We present a case of HP successfully treated with laparoscopic milking.

Case: A 21 year old G1 P0 patient came to the ER with the complaint of vaginal spotting for a day. She denied any trauma, dizziness, syncope and any other accompanying disease. Her vital signs were all within normal limits. Her last menstrual period was 5 6/7 weeks ago and she had had regular periods so far. Her transvaginal USG exam revealed a subseptus uterus and on the left side, there was a fetus with positive heartbeat, which has CRL 3.5 compatible with 6 weeks of pregnancy. Concomittantly, at the left tubal site, ectopic pregnancy with 10x8mm in size was detected. At the douglas and both ovaries, hemorrhage was detected. She was decided to taken the operating room and laparoscopic milking was performed for the left tube successfully. The pathology Result confirmed ectopic pregnancy. At the time of this writing, she had an ongoing 10 weeks of pregnancy.

Conclusion: Although HP is relatively rare; it should be kept in mind for pregnant patients during their first prenatal visit. With the collaborative efforts between MFM and Gynecology team, laparoscopic milking may be a safe option for the treatment of HP who wants to preserve their fertility.

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Successful conservative management of placenta accreta during second trimester termination of pregnancy

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A 42 years old G13 P4 woman with height previous first trimester abortions, was diagnosed with rupture of membranes at 22 weeks gestation. Medical interruption with misoprostol resulted in expulsion of the fetus without placenta. Artificial placenta removal was impossible and ultrasound examination showed the uterine wall invaded by the placenta. conservative approach was decided and placenta was left in-situ. She was given prophylactic antibiotics and two doses of methotrexate. follow up scans showed gradual shrinking of the placenta. Two months later, vaginal hysterectomy was performed because of persistant bleeding. We suggest that such a conservative management should be an option for placenta accreta in medical termination of pregnancy.

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Retrochorial hematoma as a potential cause of spontaneous miscarriage

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Introduction: The scope of causes of spontaneous miscarriages is in a big percentage unclarified.
Scope of work: To establish the frequency of a retrochorial hematoma as a special pathological substrate in the miscarriages.
Work method:
We have tested a group of 45 patients with diagnosed retrochorial hematoma who were treated during the period of 1999 to 2000 with the vital pregnancy of up to 12 weeks.
The control group consisted of 807 patients of the same gestational age with the signs of threatened miscarriage from the same period.
An ultrasound examination was the basic diagnostic procedure by which a retrochorial hematoma was diagnosed. The total number of patients of both groups was 852 of which 45 (5, 2%) were diagnosed with a retrochorial hematoma.
Results: The research has established that there is a connection between parity and gestational age in that way that the primiparas have a retrochorial hematoma in the first weeks of gestation, and multiparas have a retrochorial hematoma more often after the 10th week of gestation.
It is also shown that the coagulation factors, previous miscarriages and presence of pathological bacterial flora do not affect the occurrence of a retrochorial hematoma.
Conclusion: Ultrasound examination is the method of choice in diagnosing a retrochorial hematoma. The frequency of a retrochorial haematoma in the group of threatened spontaneous miscarriages is 5.2%. Gestational age, parity, coagulation factors and presence of pathologic bacterial flora do not affect higher frequency of a retrochorial hematoma.
A haematoma on the back wall and repeated bleedings, and not the size itself, affect higher frequency of spontaneous miscarriages.

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Selective pregnancy termination for fetal malformation in a twin pregnancy due to superfetation: A case-report

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A 23-years-old woman, secondigravida primipara, applied our Obstetrics Outpatients at 8 weeks of amenorrhoea. Ultrasonography found a single embryo corresponding to 6 weeks and 4 days of gestational age, and a second anechogen area of 7.7mm without yolk sack. Then at 15 weeks of amenorrhoea ultrasonography found a dichorionic twin pregnancy with superfetation, having an ultrasound datation the first fetus of 14 weeks +6 days of gestational age and the second 12+1. At 21 weeks +5 days of gestational age morphologic ultrasonography revealed malformations of the younger fetus of 19 weeks +5 days, in particular radial and ulnar bones hypoplasia with medial-deviation of the ipsilateral hand, and a Fallot tetralogy. Therefore, at 22 gestational weeks the woman underwent selective pregnancy termination with consequent dead fetus retention. At 38 weeks +5 days of gestational age, after labor induction with intravaginal prostaglandine because of intauterine growth restriction of the living fetus, the woman spontaneously delivered a female newborn of 2340gr with Apgar 8/9 and expelled the second dead fetus without any complication. The aim of this report is to bring attention to superfatation, that should be taken in consideration, despite the rarity of such condition.

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Progesterone and IL-1 receptors and VEGF gene polymorphisms in women with recurrent spontaneous miscarriages

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Our aim was to assess the relation between idiopathic recurrent miscarriage (IRM) and gene polymorphisms of progesterone receptor (PROGINS), interleukin-1 receptor (Pst I) and vascular endothelial growth factor (VEGF) (-634C/G and 936C/T). This case-control study comprised 89 IRM patients and 191 women with at least two successful pregnancies and no miscarriages (control group). Genomic DNA was extracted from whole blood, and polymorphisms genotyping were obtained digesting PCR products with restriction endonucleases. Genotype frequencies for PROGINS polymorphism were 72.3% T1/T1 and 27.7% T1/T2 in the IRM group and 76.4% T1/T1, 22.3% T1/T2 and 1.3% T2/T2 in the control group, without significant differences considering genotypic (p=0.48) and allelic (p=0.65) frequencies. In IL-1R1 polymorphism, there were no significant differences in co-dominant (p=0.77) and dominant (p=0.52) inheritance models and alleles (p=0.51). Genotype frequencies for 634 polymorphism did not show differences. Statistical analysis considering additive, dominant and allelic frequencies resulted in p=0.30; p=0.12 and p=0.31, respectively. For 936C/T polymorphism, frequencies were 73.8% CC, 25% CT, 1.3% TT (IRM group), and 78.3% CC, 20.9% CT, 0.8% TT (controls), showing p=0.45 (dominant model) and p=0.44 (allele frequencies). These data suggest no association between IRM and gene polymorphisms of PROGINS, IL-1R1 (Pst I) and VEGF (-634C/G and 936C/T). Besides confirming these findings, other polymorphisms must be investigated to contribute to a better understanding of IRM pathogenesis.

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Early serum leptin level and outcome of pregnancy

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Objective: To evaluate serum leptin level in patient with threatened abortion and compare to their pregnancy outcome.

Material and method:
53 pregnant women with early half of pregnancy vaginal bleeding were enrolled and their serum leptin level during vaginal bleeding episode was compared to 55 control group in same gestational age and then also compared to their pregnancy outcome.

Results: Serum leptin level was significantly different between two groups and also was related to poor outcome in patient group.

Outcome of pregnancy in patient with vaginal bleeding in early half of pregnancy was significantly abnormal (PV=0.023).

Serum leptin level was dependent directly to BMI (PV=0.0095).

Conclusion: Maternal Serum leptin level reveals pregnancy outcome in patient with early half of pregnancy vaginal bleeding.

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Effects of massotherapy using commercially available massager on blood flow of lower limbs in females

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Thrombosis is one of the most serious complications during pregnancy. Anticoagulation agents as heparin or aspirin are not always effective. In addition, the muscle strength of the lower legs is lower in women than in men, which accelerates the retention of blood in the legs and thrombosis formation. Recently, cheap and handy massagers have been developed, and self-massotherapy of the legs using such machines may be effective to inhibit thrombosis formation during pregnancy; however, physiological effects of self-massotherapy have rarely been investigated. In this study, we studied the effects of self-massotherapy on blood flow in the legs of non-pregnant women to obtain fundamental data on self-massotherapy. Five women (mean: 21.6 years) were included in this study. We applied massage with an intermittent pressure of 10.8 kPa for 15 minutes using a commercially available massager during menstruation, the follicular phase, and luteal phase. We measured blood flow velocities in popliteal arteries and veins using color Doppler flowmetry just before and after massage, and also measured skin temperatures of the lower limbs using an infrared thermometer. Blood flow in the popliteal arteries and veins increased to 5.7 and 5.2 cm/s, respectively regardless of the menstrual phase. The temperature of the skin of the lower limbs decreased by 0.5 Celsius degree in the luteal phase, although the temperature elevated by 1.3 and 0.3 Celsius degrees during the follicle phase and menstruation, respectively. These Results suggest that physiologic responses to self-massotherapy of the lower legs of women might change depending on the menstrual phase.

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Hyperthyroidism in molar pregnancy: A case report

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Objective: To report a case of hyperthyroidismo associated to molar pregnancy.

Patient(s): A 23-year-old black young woman, gravida 1 para 1, who presented with nine weeks of amenorrhea and was admitted with a history of five days of diffuse vaginal bleeding, nausea and vomiting.

Intervention(s): On examination, the patient was tachycardiac, orthostatic and febrile. Thyroid was slightly enlarge. Gynecological exam revealed presence of vesiculated material in the vaginal cavity, and a tender, soft, 15-week uterus was palpated. Pelvic ultrasound showed a heterogeneous cystic intracavitary uterine mass. Quantitative serum human chorionic gonadotropin (hCG) level was found to be significantly high. Thyroid function tests demonstrated findings consistent with hyperthyroidism. Support treatment and beta-blockers were given, and uterine evacuation by aspiration curettage under ultrasound guidance was performed. Histologic examination confirmed the diagnosis of complete molar.

Result(s): The patient experienced rapid resolution of symptoms with a dramatic decline in hCG and free thyroxine levels within a week of procedure. After 9 months of follow-up, she remained asymptomatic and her thyroid function was within normal ranges.

Conclusion(s): Human chorionic gonadotropin bears structural homology to pituitary thyrotropin. The extremely elevated levels of hCG in patients with molar pregnancy can lead to hyperthyroidism. Therapy consists of evacuation of the mole with rapid achievement of euthyroidism. Severe hyperthyroidism needs to be controlled by medical treatment such as antithroid drugs and beta-blockers.

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Level of prolactin in sudanese newborns: Relation with irds

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Objectives of this study were to determine the level of prolactin in normal healthy full term sudanese newborns and in preterms with and without irds.

Methods: 150 newborns were enrolled, 50 were healthy full term, 50 were preterm without irds and 50 were preterm with irds. Venous samples were collected and tested for prolactin using enzyme immunoassay.

Results: risk factors associated with development of irds included female sex, vaginal delivery, poor antenatal care, maternal illness and premature rupture of membranes $p<0.005$. Social class and maternal education had no influence on having irds. all those born below 28 weeks of gestation, 55% of those between 28 and 34 weeks and only 9.6% of those <34 to >37 weeks developed irds ($p=0.007$). Of those with irds 40% were below 1,000g and 60% were between 1,000 and 1,500g. out of 16 preterms born by c/s, 12.5% developed irds while out of 84 born by nsvd 57% had irds ($P=0.002$) all terms and all preterms without irds had normal prolactin levels, while all preterms with irds had low levels of prolactin. of the latter 20 (40%) were less than 28 weeks of gestation and 85% of them had very low levels of prolactin (<20ng/ml) while 70% of the 27 preterms between 28 and 34 weeks had low levels of prolactin (20-92ng/ml). conclusion: our Results may suggest that prolactin plays a role in lung maturation, and that prolactin therapy could be considered in the future management of irds.

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Influence of way of delivery on extremely low birth weight newborn babies, treated with surfactant

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Objectives: The aim of the study is to look for a correlation between way of delivery and the effect of surfactant therapy with extremely premature infants. Methods. This retrospective study includes babies born <1000g and <28g.w. in our hospital 2001–2006, treated with surfactant because of RDS. Exclusion criteria: severe inborn malformations and death before 28-th day due to severe IVH. Babies were divided in two groups - group N: 48 babies - vaginal delivery, group S: 42 babies - Cesarean Section.

Results: There are no significant differences according birth weight, gestational age, gender, severity of RDS, incidence of IUGR; kind of surfactant, timing/number of doses. Incidence of corticosteroid prophylaxis and inborn infections is definitely higher in gr. N. Babies were followed for: duration of mechanical ventilation (7 days in gr. S vs. 21 in gr. N); duration of O2 therapy (32 days in gr. S vs. 58 in gr. N); incidence of IVH: gr. S 72% IVH grade I -II, 28% - grade III-IV; vs. IVH I -II - 40% - gr. N, IVH grade III-IV -60%; incidence of BPD - gr. S 17%, vs. gr. N - 35%.

Conclusions: With ELBW treated with surfactant choosing the least traumatic way of delivery is important, ensuring smaller duration of mechanical ventilation and O2 therapy, less severe IVH, BPD.

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Preterm delivery in adolescent pregnancy

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Introduction: Adolescents as vulnerable group, tend to have poorer outcomes in pregnancy and labor with an increased risk of prematurity in comparison to older mothers. Consequences of pregnancy in this age may lead to poor physical and mental health.

Objective: To compare the rate of the preterm delivery in adolescent and adult pregnancy and to determine if adolescent pregnancies are at increased risk of poor obstetrical outcome compared with a general obstetrical population.

Methods: A hospital based retrospective cohort study of 4212 deliveries to compare the rate of preterm deliveries between adolescent and adult pregnancies.

Results: From the total number of deliveries (4,212), 5.03% (212) were adolescent. The total number of preterm deliveries was 448 (10.64% from the total number of deliveries) and 8.04% (36) of them were adolescent pregnancies. The rate of preterm deliveries in adolescent pregnancies was 16.98% (36 out of 212), compared to 10.30% in the adult pregnancies (412 out of 4,000).

Discussion: This relatively small group analysis showed that preterm deliveries were more frequent in the adolescent group, and have less favorable outcomes than those in adults. Since the study was conducted without information on cultural background, socioeconomic status or life style, further research into determinants of outcomes of teenage pregnancies is necessary.

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Twin pregnancy: Assessment of the link between pregnancy duration and the mode of delivery

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Introduction: Prematurity is one of the leading causes of perinatal morbidity and mortality, especially present in multiple gestations.
GOAL: The aim of this study was to assess the link between pregnancy duration and the mode of delivery.
Materials and methods: This retrospective study was carried out throughout a period of 12 months, with 6885 deliveries. We investigated the link between mode of delivery and pregnancy duration analyzing different twin parameters. SPSS 15 was used for statistical analysis.
Results: Analysis showed that there were 161 twin pregnancies. Out of them, 61 had vaginal delivery, while 100 had caesarean section. There was no statistical significance between the number of vaginally delivered preterm and term twins (p=0.159), while there were significantly less term than preterm twins (p=0.009) delivered by caesarean section. In both modes of delivery fetal head was the most often presenting part (vaginal p=0.000, sc p=0.000). Twins conceived by IVF/ICSI/ET and delivered preterm were significantly more frequent than those delivered on term (X2=6.751). Furthermore, significantly higher number of twins conceived by ART techniques was delivered by caesarean section. Comparing twins born on term, preterm twins had significantly lower Apgar score, as well as all anthropometric parameters in both modes of delivery. Lower Apgar scores were noticed in twins delivered by caesarean section.
Conclusion: The number of preterm and term twins delivered vaginally is similar. Twins delivered by caesarean section are usually preterm. The mode of delivery influences twin perinatal outcome, especially in those born preterm.

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Singleton and twin neonatal outcomes in premature neonates

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Objective: To compare neonatal outcomes in singleton and twin premature neonates.

Methods: A retrospective review was performed of all singleton and twin deliveries between 24 and 32 weeks + 6 days gestation that occurred from January 2003 to December 2007 in our department, in which two doses of betamethasone was administrated before a caesarean section delivery. Newborns were divided in group A (twins) and group B (singles) and reviewed concerning to the incidence of respiratory distress syndrome (RDS), intraventricular haemorrhage (IVH), periventricular leukomalacia (PVL), pneumothorax, need of mechanical ventilation, nasal continuous positive airway pressure (CPAP) and oxygen at 36 weeks and mortality. For statistical analyzes $\chi^2$ and Fisher’s exact test and t-Student were used. Statistical significance was considered when $p<0.05$.

Results: A total of 41 twins (group A) and 56 singletons (group B) newborns were analyzed. Mean gestational age was 29.1 weeks for both groups. Mean newborn weight was 1231g and 1221g for group A and B, respectively. The incidence of respiratory distress syndrome was 61.0% (n=25) in group A and 59.6% (n=31) in group B ($p=0.58$). Intraventricular haemorrhage ($p=0.18$), periventricular leukomalacia ($p=0.26$), pneumothorax ($p=0.64$) were not statistically different between the two groups. Need of mechanical ventilation, nasal continuous positive airway pressure and oxygen at 36 weeks, and mortality were also similar.

Comments: Although numbers are few, it seems that twin and singletons babies born before 33 weeks have similar neonatal outcomes when a complete cycle of pulmonary induction was performed and a caesarean section was decided.

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The perinatal outcome of adolescent pregnancy

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Introduction: Pregnancy among teenagers is a global problem and these pregnant girls are considered a high-risk group. Teenage pregnancies are associated with higher rates of maternal, fetal and neonatal complications.

Materials and methods: A retrospective analysis was carried out on the data on all mothers aged below 18 years who had delivered at the Department of Obstetrics and Gynecology, University of Szeged, between 2000 and 2008. During this 9-year period, overall 19545 births were recorded, and 174 (0.9%) of these mothers were younger than 18 years. 180 neonates were born to these adolescent mothers. We compared the data on the adolescent mothers with those on all mothers who delivered in Hungary in that period.

Results: The frequency of Caesarean section was 31.7%. 131 (75.3%) adolescents were primigravida. The mean birth weight was significantly lower in the adolescent group than in the general Hungarian population (2,856.6±724 grams versus 3,340 grams). The frequency of the premature deliveries was significantly higher in the adolescent group (25% versus 8%) and intrauterine growth retardation (IUGR) occurred significantly more often in the study group (18.3% versus 10%). The numbers of major congenital malformations (2.8% versus 4%) and of transfers to the Neonatal Intensive Care Unit (10.6% versus 8%) were not significantly different in the two groups. The umbilical cord blood pH was less than 7.2 in 15.1% of the neonates from the adolescent pregnancies.

Conclusions: A young maternal age is associated with a higher risk of an adverse neonatal outcome.

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Assessment of maternal profile correlated with early postnatal evolution of VLBW newborns (birth weight less than 1,500gr)

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Premature delivery is still a difficult attempt of neonatal modern pathology and it is under the influence of obstetrical and neonatal treatment’s changes. The authors find that assessment of antenatal maternal profile (including chronic hypertension, anemia, infections, chronic diseases and specific pathology of the uterus) could be correlated with newborns morbidity and mortality rate, especially for VLBW neonates.

This is a retrospective study over a period of 4 years performed in Neonatology Department of the Clinical Hospital of Obstetrics and Gynecology “Dr. D. Popescu” and analyzes morbidity and mortality rate in newborns weighting less than 1,500gr., depending on antenatal maternal pathology. The study group included 167 VLBW newborns and the Results were that the highest morbidity and mortality rate in this category is determined by the association between maternal infections diseases, preterm delivery and poor social conditions.

The authors conclude that survival in the study group could have been improved by using protocols for premature delivery method, antenatal corticosteroid therapy, early respiratory management (NeoPuff, CPAP) and strict infections control.

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Morbidity and mortality of preterm infants less than 28 weeks gestational age

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Prematurity less than 28W GA remains a major cause of morbidity and mortality.
Objective: study morbidity and mortality of NN ≤28W GA.
Results: 76 eligible NN (2.1% of admissions and 7.7% of preterm NN). They were 37 males and 39 females. GA was less than 26 W in 20 infants (26.3%). 25 NN (32.9%) were issued from multiple pregnancies. BW was ≤800g in 14 NN (18.2%) and higher than 1,000g in 37 NN (48.7%). Mean BW was 1,020g [450-1,400g]. Early morbidity was found in all NN represented by respiratory distress in all of them in relation with RDS in 58 NN (76.3%). Surfactant was used in 63.8% of NN with RDS. Ventilation was indicated in 71% of NN. Late morbidity consisted mainly of anemia requiring transfusion in 28 NN (36.8%) and nosocomial infections (NI) in 20 NN (26.3%). 41 NN died (53.9%). Death rate was inversely proportional to GA: 100% of 24 W, 75% of 25-26 W, 62% of 27 W and 31.4% of 28 W. Causes of death were IVH (n=17), NI (n=12), NI associated to IVH (n=5) and RDS (n=7 less than 26 W).
Conclusion: Antenatal corticotherapy, surfactant and new strategies of ventilation have contributed to improve the outcome of preterm NN with RDS. More efforts have to be performed in order to decrease factors leading to IVH and to fight against NI which remain the principle causes of deaths.

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Serum amylase level after ritodrine treatment in Japanese women of emergency maternal transport

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Objective: This study was performed to evaluate serum amylase (AMY) levels during ritodrine therapy after maternal transport.

Methods: A retrospective study was performed in 108 patients who were treated with intravenous ritodrine for more than one week. The serum AMY level was measured on admission and every week, using IFCC (International Federation of Clinical Chemistry) method. The patients were divided into the normal AMY (group A) and abnormal AMY (≥125 IU/L) (group B) groups.

Results: The AMY levels in all patients decreased significantly from 86.3±32.8 IU/L on admission to 74.9±22.8 IU/L after 2 weeks (p =0.015), and to 69.5±16.8 IU/L after 4 weeks (p =0.001), respectively. Abnormal elevation of AMY occurred in 11 of the 108 patients, and an abnormally high serum amylase level was observed within the first 7 days in 9 of the 11 patients. One patient in group B received ritodrine in combination with MgSO4. There were not significant differences between groups A and B in the doses of ritodrine on admission (83.3±44.4 µg/min and 84.8±53.4 µg/min, respectively). There were no differences between groups, in maternal age, gestational age, parity, and tocolytic score. There were no differences between groups, in the incidence of elevated liver enzyme (5/11 versus 35/97) and elevation of creatine kinase levels (1/11 versus 17/97).

Conclusion: In maternal transport, when ritodrine therapy continued for more than 1 week, 10% of patients showed an increase in AMY level. The AMY levels were not associated with an increased risk of poor perinatal outcome.

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Assessing the effect of intrauterine growth restriction (IUGR) on cerebral activity of preterm infants with the aEEG

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Background: IUGR has been correlated with increased risk for adverse neurodevelopmental outcome. The risk increases, when the growth restriction is complicated by prematurity. EEG has been proved a valuable tool in the assessment of brain damage in preterm infants, and there is good correlation between primary findings in the aEEG and EEG.

Objective: To compare the maturational rate of cortical activity between SGA and AGA prematures using aEEG.

Study design: 95 preterm infants, 30 SGA and 65 AGA were included. Patients with IVH, PVL, brain malformations and seizures, were excluded. All of them had regular aEEG recordings until discharge. Four distinct features (continuity, cyclicity, amplitude of lower border, bandwidth) were quantified according to pre-established criteria.

Results: BW was significantly lower in SGA infants compared to AGA ones (1115±230gr vs. 1,379±300gr, p<0.0001), while the GA of the two groups was comparable (30.6±1.8 vs. 29.9±2.0 wks, p=0.1). The aEEG of SGA infants was less mature at birth and it continued to develop at a slower rate compared to that of AGA. This delay was significant for the components of cyclicity (p=0.02) and bandwidth (p=0.03). With regard to continuity and amplitude of lower border, their evolution in the SGA group was slower but not significant.

Conclusion: It seems that IUGR affects negatively the cortical brain activity, as it is recorded with the aEEG, resulting in delay of its maturational process. Long-term follow-up of the IUGR preterm infants is required in order to evaluate the prognostic value of aEEG during neonatal period.

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An episode of preterm labor during pregnancy increases the risk for adverse perinatal outcome in term born fetuses

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Objective: To determine perinatal outcome among singleton term birth fetuses with an episode of preterm labor.

Material and methods: We extracted from 10404 consecutives singleton pregnancies, a cohort of 817 patients (7.9%) with a previous episode of hospital admission by preterm labor. From this cohort 659 patients (80.6%) delivered before 37 weeks (118 (14.4%) were iatrogenic and 542 (66.3%) spontaneous). Term delivered occurred in 157 (19.2%) patients. Perinatal outcome among this cohort were compared with 9587 singleton term delivered without an episode of preterm labor. T-Student test, χ², and logistic regression were used for statistical analysis.

Results: There was no significant difference for age, gender, parity and previous caesarean between both groups. Birth weight and gestational age were smaller for patients with an episode of preterm labor (3,186.93g vs. 3,313.44g; p<0.05) (38.7 weeks vs. 39.3 weeks; p<0.05). Fetuses with an episode of preterm labor showed higher risk both for a birth weight below 2,500g (8.3% vs 2.8%; p<0.05) (adjusted odds ratio 2.20 (IC 95% 1.22-3.93; p<0.05)), and for the requirement of intervention due to fetal distress (8.9% vs. 5%; p<0.05) (adjusted odds ratio 2.14 (IC 95% 1.28-3.75; p<0.05)). No differences were found for Apgar test neither first nor fifth minute.

Conclusion: Term birth fetuses with an episode of preterm labor presented lower average weight, as well as higher proportion of neonates with less than 2,500g and more requirement of intervention during labor due to fetal distress.

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Preterm delivery in madeira island – a 3 year review

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Objective: Preterm delivery affects a great number of women and constitutes a serious problem in terms of neonatal mortality and long-term morbidity. There are multiple aetiologies, influenced by a wide number of genetic, biophysical, psychosocial and environmental factors. The study was conducted to identify risk factors associated with preterm delivery and to evaluate its consequences on the newborn.

Methods: Retrospective analysis including 521 women with preterm delivery (24-37w) in Hospital Central do Funchal, from 2005 to 2007. All patients were investigated for age, race, past and present obstetric history, cervical length, gestational age and type of delivery. They were divided into 2 groups, preterm (32-37w) and early preterm (<32w). The newborns were assessed for Apgar index, NICU admittance and morbidity after 1 year.

Results: Risk factors related to the obstetrical history, genital infections, multiple pregnancy and maternal age were the most relevant for preterm birth. Premature rupture of membranes and preeclampsia were also responsible for a significant number of cases. Neonatal morbidity and mortality were inversely related to gestational age. The likelihood of survival without sequelae was further reduced in the presence of significant medical complications, namely intra-amniotic infection.

Conclusions: The patophysiological mechanisms involved in spontaneous preterm labor need to be fully understood to improve our ability to predict and diagnose these situations. Stratification of women into risk groups at an early stage is essential to determine the clinical intervention and the reduction of the preterm birth rates, thus reducing the high incidence of neonatal complications.

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Evaluation of preterm birth between 32+0-33+6 weeks of Gestation

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Objective: To evaluate perinatal outcomes of preterm birth between 32+0-33+6 weeks of gestation and over 34+0 weeks of gestation.

Methods: The neonates given birth at 32+0-33+6 weeks of gestation (142), 34+0-36+6 weeks (267), and the more than 37+0 weeks (356) was included, and the last two groups were selected by using stratified random sampling at our hospital. We evaluated the risks of preterm delivery at 32+0-33+6 weeks of gestation by comparing the perinatal outcomes, which included Apgar score, NICU admission, date of NICU admission, ventilator care, respiratory distress syndrome, bronchopulmonary dysplasia, sepsis, neonatal seizure, intraventricular hemorrhage, retinopathy, neonatal death, etc.

Result: Preterm birth at 32+0-33+6 weeks of gestation was significantly high incidence in NICU admission, longer duration of NICU admission (19.11 days) than other groups (p<0.05). Neonatal complications (low apgar score (1 min <7), NICU admission, date of NICU admission, ventilator care, respiratory distress syndrome, neonatal seizure, intraventricular hemorrhage) were statistically significant (p<0.05). There was no difference whether steroid administration or not, in respiratory complications between 32+0-33+6 weeks of gestation (p>0.05).

Conclusion: Preterm birth between 32+0-33+6 weeks of gestation had poor perinatal outcomes comparing to delivery after 34 weeks of gestation. Therefore, it is recommended that pregnant woman with preterm labor between 32+0-33+6 weeks of gestation should maintain her pregnancy as long as possible. In addition, whether steroid administration or not, in preterm delivery between 32+0-33+6 weeks of gestation, there was no difference in respiratory complications of neonates. Thus, it would be difficult to accept the idea that preterm labor at 32+0-33+6 weeks is safe.

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Premature births in sremska mitrovica general hospital in period from 1990-2008

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Introduction: Premature births still represent one of the major problems in modern perinatology. The number of factors of risk that lead to premature births has been constantly increased.

The Aim of the Work: To show the trend of premature births in the period from 1990-2008 year. The number of deliveries is about 1400 pro year. General hospital covers approximately 400000 population.

Results: The total number of births in that period was 29231. The number of premature births was 1349 (4.75%). There were 278 (20.61%) premature births aged 28-32 weeks and 1071 (79.39%) premature births aged 32-36 weeks. Perinatal mortality amounts to 3.10/o/oo-promile, and 70.71% of that number is the number of premature born children.

Discussion: Statistically significant fall of premature births from 4.46% to 2.25% has been achieved from 2005-2008 by introducing ATOSIBAN-TRACTOCILE in therapy of premature births following the strict indications-pregnancy aged 24-33 weeks gestation, contractions 4 in 30 minutes, contractions 30 sec. long, dilatation 1-3cm., shortening of cervix for 50% and more-cervicometry obligatory by ultrasound vaginal sonde and using other diagnostic methods.

Therapy was given by intra venous infusion not longer than 72 hours. These data prove that this medicine although having high price has a justifiable place in prevention of premature births.

Conclusion: Further development of prophylaxis, modern monitoring of pregnancy, introduction of up-to-date equipment in routine practice, adequate application of the latest medicines in treatment will certainly lead to more reducing of number of premature births and perinatal morbidity and mortality.

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A “Near term” infants: Is there an epidemic?

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Introduction: Near term, >34 and <36 weeks +7 days, constitute a proportion of neonates requiring special and, occasionally, intensive care.
Objectives: 1) Determine the incidence of near terms; 2) Compare complications between those born following earlier postponed delivery versus those delivered without previous threatened preterm labor.
Results: Out of a total of 2684 live births between 1 January and 31 December 2008, 161 (6.2%) were near terms; 18/161 (11.2%) were born after tocolysis. All in the tocolysis group received antenatal corticosteroids (ANCS), but none of the others. Mean gestational age (GA) was 35.3 weeks (34.5 and 35.4 for tocolysis and non tocolysis, p=0.001). Mean birth weight (BW) 2491g (2278g and 2495g for and non tocolysis, p=0.004). Average hospital stay: 12.17 days vs. 5.41 (p=0.001); admission to NICU: 72.2% vs. 26.4% (P=0.001); 16.5 admission days vs. 9.4 (p=0.001) for tocolytic and non tocolytic groups, respectively. Caesarean section (CS): 66.7% vs. 36.8% (p=0.007) for tocolysis vs. non tocolysis. There was only one neonatal death, in the non tocolytic group; morbidities and need for intensive care overlapped.
Discussion: Comparing “near terms” after tocolysis for threatened earlier preterm labor, to those born without tocolytics, they were of significant lower GA, and BW; conversely, admissions to NICU and days of stay were significantly higher. However, morbidities were similar with overlapping need for intensive care and no O2 dependency at discharge.
Conclusion: Despite lower GA, BW, longer hospital stay, these apparent good Results following postponed labor, will need confirmation by long term follow-up.

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Poster session II: Preterm delivery

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Risk calculation of preterm deliveries – application of a Bavarian model on data from the Eastern German countries

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Background: Recently, we developed multivariate risk calculation models for prediction of PTD before 37 and before 32 completed weeks of pregnancy using anamnestic and maternal characteristics. For this purpose, we used the data of the Bavarian Perinatal Registry. As social factors seem to play a crucial role in the development of PTD, we assessed now transferability of the Bavarian model on the former Eastern part of Germany where still differences in social structures exist.

Methods: We analyzed data of 223622 singleton pregnancies from the perinatal registries of the five former Eastern German countries comprising all deliveries between 1998 and 2000. The data sample was randomly split into three subsets of approximately equal size. Univariate risk factor analysis and validation of the Bavarian model were performed on subset 1. Logistic regression analysis was used to derive new prediction models on subset 1, the models were evaluated on subset 2. The new final prediction models were validated using subset 3.

Results: The Bavarian models showed an area under the curve (AUC) of 0.606 for prediction of PTD before 37 weeks and of 0.641 for PTD before 32 weeks compared with 0.625 and 0.667 for the Bavarian data, respectively. Development of new models resulted in AUC of about 0.621 and 0.645, respectively, but is still in progress.

Conclusion: Application of the Bavarian model on data from different German countries leads to the expected marginal loss in prediction quality. Implementation of additional parameters not available so far will improve accuracy in prospective studies.

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Are all late preterm deliveries (LPD) medically justified?

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Late preterm deliveries (LPD) (34 0/7 to 36 6/7 weeks) are in the rising in recent years due to increasing multiple pregnancies, better fetal surveillance and more aggressive obstetric management, leading to more neonatal admissions to NICUs.

Objective: The purpose of our study was to evaluate the reasons and justification for LPD.

Methods: We analyzed the electronic data of all late preterm infant (LPI) admissions to the NICU in our tertiary perinatal center over a period of 5 years (2003-2007) and looked for the reasons for preterm delivery.

Results: 501 mothers had 585 LPI admitted to the NICU. Table 1 indicates most of the identified pathologies.

Conclusion: From analysis of our data, only in 3.5% of LPD the predominant reason for delivery was not well identified.

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Usefulness of a dedicated clinic for pregnant women at high risk for preterm delivery

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Objective: To assess the usefulness of a dedicated clinic for pregnant women at high risk for preterm delivery in a tertiary referral unit.

Methods: Pregnancy outcome in high-risk women attending our Preterm Delivery Prevention Clinic in 2004-5 (n=268) was compared with the general population delivering at our Institution in 2004 (n=3,574). Indications for referral to the Preterm Delivery Clinic were: previous preterm delivery or miscarriage >16 weeks; history of uterine surgery; uterine abnormalities; shortened cervix; threatened preterm labor in the current pregnancy. Assessment involved vaginal and cervical microbiology, and transvaginal cervical length measurement. Patient education, targeted antimicrobial treatment, RDS prophylaxis, tocolysis and cervical cerclage were offered as clinically appropriate.

Results: The overall rate of preterm delivery was 13% (n=35) in women attending the Clinic, and 6% in controls (n=212; p<0.0001). However, preterm deliveries after 34 weeks were 32/35 in the Clinic group (91%) and 153/212 in controls (72%; p=0.01). Preterm deliveries between 24 and 33+6 weeks were 3/35 in the Clinic group (9%) and 62/212 in controls (29%; p=0.01).

Conclusions: Our Results suggest that the attendance to a dedicated Preterm Delivery Prevention Clinic does not affect the overall rate of preterm delivery, which remains higher in high-risk women compared to controls. However, it has the potential to shift preterm delivery towards gestational ages after 34 weeks, which are associated with a significantly lower perinatal mortality and morbidity.

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Antenatal counseling by a dedicated in-patient counseling team in a tertiary centre: A 15-month experience

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Objective: Antenatal counseling is performed for a variety of reasons. A dedicated in-patient antenatal counseling team was established in our hospital (a tertiary referral centre in Hong Kong). This study reviews the counseling performed by our team over a 15-month period.

Methods:
Records of all in-patient antenatal counseling requests (computer-logged) from January 2008 to March 2009 were retrieved. Clinical features, content of counseling and outcome were reviewed.

Results:
115 in-patient antenatal counseling requests were received during the study period. 94% (108/115) were for prematurity (gestation <36 weeks), including 4.6% at the lower limits of viability (gestation 22-24 weeks). The remaining requests included congenital anomalies (3.4%) and vaccine refusal (2.6%). Counseling was performed within the same day of request in 87%, while 5.2% were performed between 24-48 hours. Counseling was not performed in 7.8% because of urgent delivery. 34% counseling took place in the delivery suite, and 66% took place in the antenatal ward. All counseling was performed by an experienced neonatologist together with a neonatal nurse, and major issues concerning the fetus were discussed. Photographs of the neonatal unit and case-studies were shown when considered appropriate (89.4%), and was well-accepted by all parents. 5.2% required >1 counseling sessions. 38% women counseled for prematurity delivered within 48 hours.

Conclusion:
The major indication for in-patient antenatal counseling is prematurity. Counseling should be performed promptly as a significant proportion deliver within 48 hours of presentation. A dedicated and experienced antenatal counseling team is essential. Photographs and case-studies, when used appropriately, can improve understanding and is well-accepted.

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Teenage Pregnancy – High Risk Pregnancy?
2 Years Retrospective Study

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Introduction: Most teenagers don’t plan to get pregnant, some do. High teen birth rates are an important concern because teen mothers and their babies face increased risks to their health and their opportunities to build a future are diminished. Teenagers are more likely to have anaemia, high blood pressure, growth-restricted infants, preterm labor, infant homicide, domestic violence, substance abuse, low maternal education and socioeconomic status.

Methods: Retrospective analysis of clinical files from all pregnant with ≤ 17 years old, followed in the High Risk Appointment of the Hospital of Faro, in 2007 and 2008.

Results: In the years 2007 and 2008 our hospital had 6149 live births, 107 of which in teenagers. At the Hospital’s appointment we followed up 127 teenagers, with an average age of 16 years old. Half of their mothers had been pregnant during teenage years. 64% had dropped school, either before or during the pregnancy, being the average age of scholar the 7th grade. Most of them were Primigesta; didn’t do any contraception (64%) and 45% smoked or consumed other drugs. The first appointment was in average at 17 week. The majority didn’t have any pathology previous to pregnancy nor complications during it or at labor. The birth was mainly vaginal at term.

Conclusions: Pregnancy during adolescence years implies a double effort on physiologic and psychological adaptation and conciliation of 2 converging realities. Insist on contraception and early seek for prenatal care is of major importance.

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Material and methods: A retrospective observational study 120 patients who received 184 cerclages (from 46,499 deliveries) during 1998-2008 at the University Hospital Virgen de las Nieves was made in which medical histories of patients, type of cerclage received, proportion of preterm delivery and weight birth were analyzed.

Results: Mean age of patients was 26.4±5.7 years, gestational age at birth 241±47.7 days and fetal birth weight was 2493.8±1115.5g. 125(68%) patients had a history of preterm birth or late abortion and 7(3.8%) had received a previous cervical surgical treatment. 22 patients (12%) had an uterine malformation (double uterus/bicornuate). 30(16.2%) patients had no history of risk. There were performed 154(83.7%) elective, 10(5.4%) therapeutic, 16(8.7%), emergency and 4(2.2%) double cerclages. 168(91.3%) achieved by Mc Donald technique and 16(8.7%) by Shirodkar. Proportion of delivery <34, <37 and ≥37 weeks: 24.6% (38 cases), 33.7%(52) and 66.3%(102) in elective; 33.3%(3), 33.3%(3) and 66.7%(7) in therapeutic; 100%(16), 100%(16) and 0 cases in emergency; 50%(2), 50%(2) and 50%(2) in double cerclages respectively. Average time to pregnancy: 250±38.7 days in elective, 255.8±29.11d in therapeutic, 155.13±25.11d in emergency and 203±63.1d in double cerclage. Mean birth weight: 2699±994.5g in elective, 2689.8±847.55g in therapeutic, 652.19±334.8g in emergency and 1500±992.4g in double cerclage.

Conclusions: Elective and therapeutic cerclages appear to be effective techniques for reducing the rate of prematurity in patients with risk factors of preterm delivery but not emergency cerclage according to our Results.

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Pregnancy outcome associated with cervical cerclage placement in a Brazilian tertiary center

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Objective: To evaluate the pregnancy outcome of 148 women who underwent cervical cerclage for prevention of preterm birth.

Methodology: Through a retrospective study of medical records, we reviewed all cases of women who underwent cervical cerclage for prevention of preterm birth in Instituto Fernandes Figueira (Rio de Janeiro, Brazil) from January 2002 to December 2005. Twin pregnancies were excluded. We also analyzed the association of several obstetric variables (previous history of cervical conization, late miscarriage, premature birth, neonatal death and uterine curettage; cervical dilation and bulging membranes at the time of the procedure; prelabor membranes after the procedure) with poor outcomes (birth <32 weeks or late miscarriage).

Results: Late miscarriage occurred in 4.7% (n=7) of cases; birth happened between 22 and 31+6 weeks in 14.2% (n=21), between 32 and 36+6 weeks in 23.7% (n=35) and after 37 weeks in 57.4% (n=85) of cases. The stillbirth and early neonatal death rates were 2.1% and 5%, respectively. The risk factors analysis for preterm birth before 32 weeks or late miscarriage showed statistical significance only for bulging membranes at the moment of the cerclage procedure (p=0.04) and premature rupture of membranes after the surgical procedure (p=0.00).

Conclusion: Our Results revealed that 80.1% of pregnancies in which cervical cerclage were performed went over 32 weeks. The main risk factors observed for births under 32 weeks were bulging membranes at the time of cerclage and prelabor membranes rupture after the procedure.

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Effect of 2 stitches vs. 1 stitch on the prevention of preterm birth in emergent cerclage for amniotic sac prolapse

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Objective: The objective of the study is to compare outcomes after 1 stitch versus 2 stitches cerclage in the treatment of women with amniotic sac prolapse in the second trimester.

Study design: This is a retrospective study at the investigators’ institution over a 20-year period through 1988. The medical record was provided by the files of 63 women who received emergent cerclage for fetal membrane bulging between 16+0/7 and 27+0/7 weeks of gestation. Gestational age at delivery, prolongation of pregnancy, the frequency of preterm birth (<34, 28 weeks of gestation) and clinical characteristics were evaluated.

Results: 31 patients (70%) received 1 stitch, and 14 patients (30%) received 2 stitches. The median width of amniotic sac prolapse was similar as 3.0 cm in both groups and there were no demographic differences. Mean gestational age at delivery in weeks was 27.5±8.1 and 33.6±6.1 for 1 vs. 2 cerclage (p=0.016), respectively. There were fewer deliveries before 34 weeks in the 2 stitches cerclage group (23(74%) compared with 5(36%), p=0.021) as well as 28 weeks (15(48%) compared with 1(7%), p=0.008). There was also a significant difference in the median prolongation of pregnancy: 31 days in the 1 stitch group (interquartile range 5-89) compared with 93 days in the 2 stitches group (interquartile range 66-111) (p<0.008).

Conclusion: 2 stitches cerclage may be more effective method for preventing preterm delivery than 1 stitch cerclage in pregnant women with amniotic sac prolapse.

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**Outcome-monitoring of patients with and without cervical cerclage – a comparative study**

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Introduction: During pregnancy the competent uterine cervix presents a mechanical barrier between the vagina and the contents of the uterus. Shortening of the cervix is a physiological process at the end of pregnancy but the cervix that appears short preterm is at risk to dilate premature and therefore presents a great risk factor for preterm birth. There is evidence that the cervical cerclage may be beneficial in patients with high risk for preterm delivery by prolonging gestation.

Objective: This study investigates whether the use of cervical cerclage has an effect on continuance of pregnancy and fetal outcome compared to women treated conservatively.

Methods: In this retrospective study 57 patients who received cervical cerclage between 2003-2006 built the case group that was compared with 44 patients of the control group treated observantly with the same diagnosis. Comparison between case and control group solely included singleton pregnancies.

Results: In singleton pregnancies cerclage was placed significantly earlier in pregnancy (Â¬ 18+4) than cervical incompetence was diagnosed in singleton pregnancies of the control group (Â¬24+5). Single pregnancies of the control group lasted significantly longer (Â¬ 36+1) than those of the case group (Â¬ 33+3). There was no significant difference in the number of live-births and stillbirths between the groups. Newborns of the control group had significantly better APGAR- scores at one, five and ten minutes post partum.

Conclusion: The present study did not show an improvement of continuance of pregnancy and fetal outcome by using cervical cerclage.

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Does the timing of elective cerclage effects perinatal outcomes

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Objective: We aimed to investigate the effect of the timing of elective cerclage on duration of pregnancy and perinatal outcomes.

Methods: We retrospectively enrolled 36 patients who underwent elective McDonalds cerclage between 13-21 weeks of gestation with at least one second trimester pregnancy loss due to cervical incompetence. Group 1 (n=21) and group 2 (n=15) included patients with cerclage performed before 15th gestational weeks and after 15th gestational weeks, respectively. We compared duration of pregnancy and perinatal outcomes between two groups by Mann-Whitney U and Chi Square tests.

Results: Mean age was 29.2±5.1SD in group 1 and 29.6±4.2SD in group 2 (p=0.89). Number of painless second trimester loss was 1.43±1SD in group 1 and 21.58±0.3SD (p=0.49) in group 2. Median (minimum-maximum) weeks of gestation at birth were similar between two groups [39(26-40.3) in group 1 and 38.2(25-39) in group 2 (p=0.21)]. 73.3% of patients in group 1 and 71.1% in group 2 delivered at term (p=0.9) and 93.3% of patients in group 1 and 81% in group 2 delivered after 34th gestational weeks.

Conclusion: Performing elective cerclage before 15th gestational weeks did not improve duration of pregnancy and perinatal outcomes compared to elective cerclage after 15th weeks.

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A randomized controlled trial of vaginal lactobacilli vs. vitamin C as adjuvant treatment for bacterial vaginosis in pregnancy

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Objective: Bacterial vaginosis (BV), characterized by absent Lactobacilli and an abnormal presence of anaerobes, is associated with an increased risk of preterm delivery. Vaginal lactobacilli and vitamin C could be useful adjuvants in the treatment of BV.

Materials and methods: 100 pregnant women with BV referred to our Preterm Delivery Clinic between January 2006 and June 2008. In addition to standard clindamycin treatment for 6 days, women were randomized to receive a 12-days course of vaginal tablets with either L. acidophilus 40mg (Group A) or vitamin C 250mg (Group B). The main outcome was the presence of vaginal Lactobacilli on a follow-up vaginal swab performed after 3-5 weeks.

Results: 50 women were randomized to each treatment group, at 15-33 weeks of gestation. On follow-up, a normal lactobacillary flora was present in 80% and 87% of women in Group A and B, respectively. Pathogenic bacteria were grown in 32% and 24% of samples, respectively. The rate of preterm delivery before 37 or 34 weeks was 25% and 4% in Group A, and 26% and 6% in Group B, respectively. All the differences were not statistically significant.

Conclusions: The rate of lactobacillary recolonization was high, and treatment was equally successful in both groups. Further research is needed to compare lactobacilli and vitamin C against placebo in pregnancy, and to determine if the have any effect on the preterm delivery rate.

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Benefit of tocolytic drugs use – a retrospective study in a tertiary care unit

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Preterm birth remains one of the most serious problem in perinatal medicine and is associated with an increased risk of neonatal morbidity. Delaying delivery with tocolysis allow administration of a complete course of antepartum glucocorticoids which in turn may improve maturation of developing organs and systems. We present a retrospective study from 2005 to 2008 of inhibition of preterm labor in a tertiary care unit with tocolytic drugs (Atosiban and others). We concluded that the use of a single or more courses of Atosiban improved the outcome in women with early gestational ages and also in those which had not yet received a full course of antepartum glucocorticoids.

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The effects of sivelestat sodium hydrate on suppression of uterine contraction resulted from intrauterine infection

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Objective: Inflammatory cytokines resulted from chorioamnionitis has been suggested to have a important role on premature delivery. This time we examined tocolytic effects of the neutrophile elastase inhibitor (a sivelestat sodium hydrate) using an intrauterine infection sheep model administered Lipopolysaccharide (LPS) into the intra-amniotic compartment.

Methods: With the chronically instrumented ewes, Group A (four ewes) administered an antibiotic after LPS administration. Group B (four ewes) administered a neutrophile elastase inhibitor (0.2mg/kg/24h) with an antibiotic after LPS administration. Group C (four ewes) was a sham operation group.

Uterine contraction was evaluated by fetal tracheal pressure and maternal and fetal blood concentration of PGE2, IL-6, IL-8, TNF-α before and after LPS administration were measured.

Result: 1) All ewe of Group A delivered babies within 72 hours, but only one sheep of Group B delivered and uterine contraction was suppressed about 60% versus Group A.
2) Maternal IL-6, IL-8 and TNF-α level of Group A was significantly elevated and each maximum concentration was 0.6pg/ml, 2680pg/ml, 9pg/ml, but there was no significant changes in Group B and C.

Conclusion: Neutrophile elastase inhibitor might to become one of useful strategy to prevent premature delivery resulted from intrauterine infection.

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Ampicillin effect on cervical mucus level of Interlukins and prevention of preterm labor

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This study aimed to evaluate the effects of antibiotic therapy on the mucus levels of IL6 and IL8 in uterine cervix and its efficacy in prevention of preterm labor.

Materials and Methods: This clinical trial was conducted on 58 primigravid women in 26-32 weeks gestational age admitted with the diagnosis of preterm labor. Patients were randomly divided to two groups. Group A (n=28) received 12mg IM injection of betametasone per day plus magnesium sulfate drips. Group B received IV injection of Ampicillin 2gr per 6 hours in addition to the regimen administrated for group A. Endocervical mucus samples were taken before and 72 hours after treatment in each patient and the levels of interlukin 6 and 8 were measured in each sample. Data were analyzed with SPSS-12 using t-test, 2, and regression analysis was done.

Results: Mean levels of IL6 showed a non significant decrease in group B after intervention and was not different before and after treatment in group A. The levels of IL8 were shown to be not significantly different before and after treatment in both groups (p=0.734). Multi-variant analysis showed that the rate of premature delivery in the first week after treatment in group A was three fold in comparison to group B.

Conclusion: Ampicillin reduces the level of IL6 in cervical mucus and can prevent the preterm delivery during the first week after treatment.

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Celebrex versus magnesium sulfate to arrest preterm labor; Randomized trial

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Background: Despite the encouraging Results of recent studies (25) demonstrating improved methods to predict prematurity and prevent preterm labor, the incidence of preterm delivery has remained stable during the last 20 years.

Aims: To compare oral celebrex with intravenous magnesium sulfate as Mgso4 tocolytic.

Methods: This was Mgso4 randomized study of patients who were between 24 and 34 weeks of gestation with preterm labor. 104 pregnant woman with preterm labor were randomly assigned to receive either daily oral celebrex (100mg/BD) or intravenous magnesium sulfate for maximum of 48 hours. Outcome variables included delay of delivery for 48 hours and the incidence of side effects. Data were analyzed by using the Student t test, Mann–Whitney U test, 2 test. Sample size calculations were based on previous studies of tocolytic efficacy.

Results: one hundred four patients were randomly assigned (52 received celebrex and 52 received magnesium sulfate). Arresting labor for 48 hours was for 48 hours in 42 (81%) and 45 (87%) of the patients in the celebax and magnesium sulfate groups, respectively p value (0.298). There was no difference between the groups over the course of the study in cervical dilatation, amniotic fluid index.

Conclusion: There was no difference between oral celebrex and intravenous preterm labor in arresting preterm labor.

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Efficacy and safety of atosiban therapy of preterm labor with twins

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Objective: The aim of this study was to evaluate the efficiency and safety of the oxytocin receptor antagonist atosiban in the treatment of preterm labor with twin pregnancy.

Study design: We analyzed 77 twin pregnancies with signs of preterm labor between 26 to 34 weeks gestation. The efficiency of atosiban was assessed in two time frames: 1) within the first 48 hours, and 2) within the first 7 days from initiating the atosiban therapy. Atosiban was effective if delivery was delayed for more than 48h or for more than 7 days. Maternal safety was analyzed and adverse effects of atosiban therapy were also recorded.

Results: Atosiban was effective in 82.5% of cases for delaying delivery for 48h. This drug was effective in 75.0% of the cases for delaying delivery for more than 7 days. Overall, the delivery was delayed 368±42h, mean gestational age of delivery was 31.8±3.6 weeks, but 41% of twins, were delivered at 37 weeks. Birth weight was 2140±140g with mean Apgar score of 5` 7.6±2.1. The incidence of operative type of delivery was 45%. The maternal side effects were registered in 10.5% of cases, mostly nausea, vomiting and headache.

Conclusion: Atosiban is an effective and safe drug for the acute treatment of preterm labor with twin pregnancy. Maternal side effects of atosiban are rare and minor.

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Efficacy and safety of β²-agonist as compared with atosiban in treatment of preterm labor of singleton pregnancies

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Objective: The aim of this study was to evaluate the efficacy and safety of the β²-agonist and oxytocin receptor antagonist atosiban in the treatment of preterm labor of singleton pregnancies. We also analyzed maternal and fetal side effects of β²-agonist and atosiban.

Study design: We analyzed 194 pregnancies with signs of preterm labor between 26 and 34 weeks gestation. Efficacy of tocolytic treatment was defined in two time frames: 1) as delaying delivery for more than 48h since starting the intravenous therapy with atosiban or β²-agonist and 2) delaying delivery for more than 7 days. The prevalence of categorical side effects between treatment groups was analyzed using a χ² test.

Results: Atosiban was effective in 13.6% of cases for delaying delivery for more than 48h and β²-agonist in 12.8% of cases (p=NS). Atosiban was effective in 45% of the cases for delaying delivery for more than 7 days but β²-agonist in 42% of cases (p=NS). The prevalence of categorical side effects was similar with both drugs, with exception of palpitations (15.3% in β²-agonist group vs. 2.2% in atosiban group, p<0.05), tachycardia (72.0% in β²-agonist group vs. 1.3% in atosiban group, p<0.01) and tremor (11.0% in β²-agonist group vs. 1.4% in atosiban group, p<0.01).

Conclusion: Atosiban is superior to the β²-agonist with respect to safety and maternal tolerability for the acute treatment of preterm labor. Efficacy of both drugs is similar in the acute treatment of preterm labor of singleton pregnancies.

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Antenatal exposure to histologic chorioamnionitis and positive *Ureaplasma sp.* in the airways of ventilated preterm infants is associated with elevated markers of a systemic inflammatory response

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*Ureaplasma* sp. is one of the commonest organisms associated with histologic chorioamnionitis and prematurity.

The objectives of this study were, (1) to identify the characteristics of a subset of ventilated preterm infants who were positive for *Ureaplasma sp.* and, (2) to determine which factors could be used as markers to distinguish between colonization and infection of the respiratory tract.

Tracheal aspirates were obtained within the first 72 hours of life and tested for *Ureaplasma urealyticum* (U. u.). Bloods were collected for measurement of inflammatory markers. Placental tissues were sent for histopathological examination.

Forty ventilated preterm infants with a mean gestation of 27.4±3.0 wk and birth-weight of 936±274g were enrolled. U. u. was positive in the tracheal aspirates of seven (17.5%) infants. There were no significant differences between U. u. positive and negative infants in the white blood cell count, IT ratio, C-reactive protein (CRP), maximum oxygenation index, duration of ventilation and oxygen requirement, development of chronic lung disease and mortality. Four (67%) U. u. positive infants and 12 (44%) U. u. negative infants had exposure to chorioamnionitis. Exposure to chorioamnionitis was associated with elevated white blood cell count and CRP. U. u. positive, chorioamnionitis positive infants had higher CRP than U. u. positive, chorioamnionitis negative cases.

U. u. positive ventilated premies were not significantly different than U. u. negative infants in the systemic markers of inflammation, early respiratory status and later outcomes. U. u. positive infants with exposure to chorioamnionitis were more likely to have a systemic inflammatory response.

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Neonatal Morbidity in less than 1500g premature infants related to clinical chorioamnionitis

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Objective: To find if there are correlation between maternal clinical chorioamnionitis and acute morbidity and mortality in premature.

STUDY DESIGN. A multicentric prospective case-control study in premature infants (≤1500g) matched by gestational age. 328 premature (165 cases and 163 controls) from 12 hospitals.

Results: In the chorioamnionitis group intubation during resuscitation was needed more often (53.0% vs. 35.8%; p=0.002), Apgar at five minutes was lower (p=0.001), early sepsis was more frequent (10.4% vs. 1.2%; p=0.001) and there was more infants born indoor (95.1% vs. 89.1%; p=0.039), from single gestations (76.4% vs. 65.6%; p=0.032), vaginal deliveries (47.3% vs. 33.3%; p=0.01) and with normal intrauterine growth (98.1% vs. 84.7%; p=0.035). Older mother (32.5 y vs. 30.8 y; p=0.006), premature labor (67.3% vs. 25.8%; p=0.001), premature rupture of membranes (61.3% vs. 25.8%; p=0.001) and antibiotic treatment (88.5% vs. 52.3%; p=0.001) were associated with chorioamnionitis. Follow up during 2 years is being performed in both groups to compare neuropsychological development.

Conclusion: If gestational age is controlled, chorioamnionitis is associated with neonatal depression and early sepsis but not with other complications link to prematurity.

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**Neonatal Septicemia – retrospective study at premature newborns**

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Objective: Within this retrospective study the authors aimed to analyze the risk factors of the disease by grade of premature and starting age, correlated, on one hand, with clinic and biologic signs and on the other hand with morbidity and mortality.

Material and method:

The study was carried out on a period of one year (2008), on a lot of 38 premature newborns, hospitalized, selected by anamnestic, clinic, epidemiologic and biologic criteria. The prevalence of the disease was 4.03%.

Results: Neonatal septicemia with early start was present at 14 cases (41%), with extremely serious clinic signs. There were 9 cases associated with materno-fetal infection (64.28%), 5 cases with rupture membranes at 18 hours (35.72%). The mortality was high in 5 cases (14.71%), at big premature with intrauterine chronic affection and history of materno-fetal infection. The most present germs were: Serratia Marcensens, Pseudomonas Aeruginosa, and Staphyloccocus coagulasonegative.

Septicemia with late start was present at 18 cases (52.64%) having a higher prevalence at premature with gestational age lower than 32 weeks and birth weight lower than 1,500g, with long hospitalization and associated malformative pathology. the same germs were involved.

Both groups presented classic signs of septicemia. Beyond positive hemoculture were present: positive PCR with values between 8.92mg/l and 220mg/l, leucocitosys between 17240/mm³ and 44000/mm³, thrombocytopenia between 15000/mm³ and 120000/mm³.

Conclusions: Neonatal septicemia is a serious affection with high mortality (14.71%) at premature newborns even if antibiotherapy was early started.

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Interleukin-8 in preterm deliveries: Possible marker of infection

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Introduction: Preterm birth is hypothesized to be an inflammatory response disease. Inflammatory cytokines have been reported to be associated with infection, preterm contractions and preterm deliveries.

Purpose: This study focuses if serum level of proinflammatory cytokine interleukin-8 might be used as biochemical marker of infections in patients with clinical symptoms of pre-term deliveries.

Methods: The study included 80 pregnant women of 24-36 gestational weeks with symptoms of pre-term delivery. Measurement of interleukin-8 in the patients’ serum were performed by ELISA technique.

Results: The mean value of interleukin-8 in the investigated group of patients (n=45) was 18.13 pg/ml versus 5.20 pg/ml in the control group (n=35).

Conclusions: The Results of the study indicate that serum level of interleukin-8 using ELISA techniques measured in serum, might be used as noninvasive marker of infections in pregnancy, as well as marker of the increased risk of preterm deliveries. The future aim would be to consider their impact on treatment decisions - termination of pregnancy or continuation.

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Villitis and chorioamnionitis: Association with placental adenoviral detection

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Background: Adenovirus is a known pathogen associated with upper airway tract infection and conjunctivitis. Certain serotypes (Ad19, Ad37) have shown tropism for the genital tract causing cervicitis in women and urethritis in men. Adenovirus has been isolated from the amniotic fluid more frequently compared to other viruses. Aim: To study the prevalence of placental adenoviral detection in association to preterm birth and histological infection (villitis and chorioamnionitis)

Methods: We prospectively collected 216 placental samples from preterm and term deliveries. Placental adenoviral genome was detected by PCR analysis. Histological chorioamnionitis was indentified by Heamatoxylin-heosin stain and villitis immunohistochemically against common leukocyte antigen (LCA)

Results: Of the 219 placentas 87 were preterm and 129 term. Placental adenoviral genome was isolated in 64/219 (29.6%) of placentas. Adenovirus was significantly more prevalent in preterm placentas (40%) compared to term (22.4%) (p=0.002). Histological evaluation was carried in 99 placentas (56 preterm and 43 term). In adenovirus positive samples villitis was present in 22/47 (46.8%) and chorioamnionitis in 13/47 (27.7%). In the adenovirus negative samples villitis was present in 15/52 (28.8%) and chorioamnionitis in 11/52 (21.2%). In the total sample there was no significant association between adenoviral detection and histological infection. Nevertheless in the subgroup of preterm placentas villitis and chorioamnionitis was more frequent among adenovirus positive placentas compared to adenovirus negative (p=0.005 and 0.03 respectiveley).

Conclusion: Placental adenoviral detection is associated with histological infection in preterm placentas suggesting a possible association between adenovirus and premature labor.

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Perinatal outcomes in women with intra-amniotic inflammation in preterm labor with intact membranes

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Objective: To evaluate the outcome of pregnancies complicated with intra-amniotic inflammation in preterm labor with intact membranes.

Methods: 93 pregnant women with preterm labor and intact membranes (22.0-36.0 weeks of gestation) were included in our study. Transvaginal cervical length was measured on admission and transabdominal amniocentesis was performed within the first 48 hours at admission. Positive amniotic fluid cultures defined intra-amniotic infection. High levels of IL6 defined intra-amniotic inflammation. To determine the best cutoff point of IL6, a ROC curve was constructed. Considering inflammatory status, perinatal outcomes were evaluated and compared.

Results: Intra-amniotic infection and inflammation rates were 14% and 28%, respectively. ROC curve analysis showed that best cutoff value for IL6 was 13.4ng/mL which was comparable to the cutoff of 11.3ng/mL reported previously by other authors. Regardless of the intra-amniotic microbial status, perinatal outcomes in women with intra-amniotic inflammation were worse than those who did not: Gestational age (GA) at delivery (weeks, mean and SD) was 35.8 (4.0), 29.5 (4.8) and 26.9 (3.9) for women with negative culture and low IL6 (n=65), negative culture and high IL6 (n=15) and positive culture (n=13), respectively (p<0.001). Amniocentesis to delivery interval (days, mean and SD) was 34.7(29.1), 18.0(33.5) and 4.9 (5.0) in the same groups (p<0.001). Birthweight (grams, mean and SD) was 2661 (901), 1463 (778) and 1077 (548) (p<0.001) and admission to NICU was (n (%)) 25 (39.1%), 11 (73.3%) and 10 (76.9%), respectively (p =0.003).

Conclusion: Intra-amniotic inflammation is a risk for adverse perinatal outcomes despite of negative amniotic cultures.

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Screening and detection of infection/inflammation in management of preterm labor

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Objective: The purpose of this study is to find and treat bacterial vaginal pathogens, evaluate markers predicting infection/inflammation and find the optimal time for termination of pregnancy in cases of PPROM in gestational age <30th week.

Methods: We evaluated the basic infection markers (CRP, leucocytes, neutrophils), bacterial culture including sexual transmitted diseases (STD). We combined the Results with novel markers of infection (MMP-8, IL6, sRAGE) and added also cytological cervicovaginal smear using Bethesda classification 2001. Association between parameters were determined by using Pearson and Spearman correlation coefficients.

Results: The higher incidence of bacterial vaginosis, STD and B-streptococci were detected in the group of threatened premature labor in comparison with the group of term deliveries. Action of microorganisms on the vaginal epithelium develop the typical morphological changes in the cell nucleus and in the cytoplasm. Chorioamnionitis detected by histological examination in 72% vs. 35% in term deliveries (p=0.005) and funisitis 48% vs. 22% (p=0.009). In pregnant women with threatening premature labor and PPROM sRAGE serum levels were significantly increased in comparison to healthy pregnant women (818.85±328.52 pg/ml vs. 668.80±295.73 pg/ml, p<0.05). sRAGE correlated significantly negatively with leukocyte count, but not with CRP. In cases of increasing infection markers and detection of bacterial vaginal pathogens, after the corticosteroid stimulation the pregnancies were terminated mainly by caesarean section.

Conclusion: The combination of vaginal screening of bacterial pathogens, detection of markers of infection/ inflammation, ultrasound measurement of cervical length give good information for optimal timing for termination of pregnancy and saving preterm delivered infants.

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Oligohydramnios at the 2nd trimester of pregnancy – what’s prognosis?

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Introduction: A significant reduction in the amount of amniotic fluid correlates with an increased rate of both perinatal morbidity and perinatal mortality. The causes of second trimester oligohydramnios include preterm premature rupture of membranes (PPROM), fetal anomaly precluding fetal urination, amniocentesis or a chorionic villus sampling, and more rarely intrauterine growth retardation. The efficacy of treatment depends on the cause of the oligohydramnios and the gestational age of diagnosis. However if it persist, the outcome, regardless of its cause, is uniformly poor.

Objective: To characterize neonatal and maternal morbidity and mortality rates in pregnancies complicated by oligohydramnios in the second trimester.

Methods: We reviewed maternal and neonatal outcomes of women with oligohydramnios in the second trimester of pregnancy at our institution, from 1996 to 2008. Outcomes evaluated included neonatal and maternal morbidity and mortality, and maternal and neonatal length of stay.

Results: During the study interval, a total of 99 women were identified. Mean maternal age was 28.9 years. Forty seven percent of the women in the study were nulliparous. Mean gestational age of oligohydramnios diagnosis was 23.6 ± 3.5 weeks, and the majority had PPROM. The average length of latency was 24.5 days. Perinatal/neonatal mortality was 14.1%. The most frequent neonatal morbidity was hyaline membrane disease and hyperbilirubinemia. Maternal morbidity was chorioamnionitis and endomyometritis. Eighteen percent of pregnancies had medical termination.

Conclusions: Despite of the poor prognosis of the second trimester oligohydramnios, we concluded that the conservative management and serial sonographic evaluations can achieve better Results in a few selected numbers of cases.

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Preterm ruptured membranes – infectious pathology risk factors at a lot of premature newborns

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Objectives: Evaluation of the premature ruptured membranes incidence in an neonatology services, identification of microbial agents involved in producing infections.

Material and Method The study was carried out in the Clinic of Premature and Neonatology, during 2 years, on a lot of 56 premature newborns.

Selection criteria were anamnestic, clinic and paraclinic.

Results: From the studied lot, 44 newborns (78.5%) have had a birth weight of 1,000-1,500 grams, with gestational age between 28 and 35 weeks, and 12 newborns (21.5%) under 1,000 grams, with a gestational age of 26-30 weeks. Distribution by gender showed a number of 32 (57.2%) male newborns and 24 (42.8%) female ones. Regarding the origin environment, 36 (64.2%) came from rural environment and 20 (35.8%) from urban one. The most frequent identified risk factor was: ruptured membranes over 18 hour – in 15 cases (26.7%). Most frequently involved infectious agents were staphylococcus aureus and gram negative bacillus. Bacterial infections were localized in 31 of the cases (55%), represented by: omphalitis, rhinitis, blepharoconjunctivitis and systemic infections in 25 cases (45%).

Conclusions: The risks for newborns to develop infections increases with the prolonging of premature ruptured membranes labors’ duration and the newborns’ low birth weight. Prolonged labor in cases with premature rupture of membranes indicates the need for starting early antibiotic therapy.

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Increased expressions of MMP12 and IL8 in preterm choriodecidual membrane with labor

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Aim: To identify increased expressions of matrix metalloproteinase 12 (MMP12) and interleukin 8 (IL8) in choriodecidual membranes of patients in preterm labor.

Methods: Choriodecidual membranes were separated from fetal membranes of patients in preterm labor (n =18) and term labor (n =15), and Total RNAs were from the choriodecidual membranes. To identify increased expressions of MMP12 and IL8, cDNA microarray, real-time quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR), western blot analysis, and immunohistochemistry were performed.

Results: Of the 31,207 genes screened, 130 were upregulated in the preterm labor group compared with the term labor group (p<0.05, >twofold change); among these genes, the expressions of MMP12 and IL8 were increased. Real-time qRT-PCR showed that expressions of both genes were significantly higher in the preterm labor group than in the term labor group (p<0.05, respectively). Western blotting showed that expressions of MMP12 protein were significantly higher in the preterm labor group than in the term labor group (p<0.05), IL8. On the other hand, immunohistochemistry showed that the expressions of MMP12 and IL8 were stronger in choriodecidual membranes of the preterm labor group than the term labor group.

Conclusion: The expressions of MMP12 and IL8 were increased in the choriodecidual membranes during preterm labor, suggesting that these genes may be involved in the mechanism of preterm labor.

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Retrospective analysis of expectant management of previable rupture of membranes

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Objectives: To evaluate pregnancy outcomes after previable premature rupture of membranes (PROM).

Study Design: The study included all pregnancies with previable PROM at 14-24 weeks of gestation that were admitted at the Department of Obstetrics of Hospital de S. João, Porto, Portugal, between January 1999 and October 2008 (n=76). Data on gestational age at PROM, latency period, maternal risk factors, antenatal care, obstetrical and neonatal outcomes, were collected from clinical charts.

Results: Rupture of membranes occurred at 14-19 weeks gestation in 47 cases (61%), at 20-24 weeks in 24 (32%) and information was missing in 5 cases (7%). Among factors commonly related with previable PROM, we found amniocentesis (16 cases; 21%), trauma (1 case), gestation with intrauterine device (1 case) and gestation with cervical cerclage (1 case). Twenty-one pregnancies with previable PROM (27.6%) were medically terminated, 23 (30.3%) aborted spontaneously before 24 weeks, 8 (10.5%) left hospital with evolutive gestation (without posterior information) and 24 (31.6%) maintained their pregnancy beyond 24 weeks of gestation. Concerning this later group, 4 fetuses died in utero and 4 died in early neonatal period. Among the 24 pregnancies that evolved beyond 24 weeks, 15 newborns (63.5%) were delivered before 32 weeks.

Conclusions: The prognosis of previable PROM was generally poor, less than one-third of pregnancies reached viability threshold, perinatal mortality and prevalence of very preterm were high. Despite recent advances in perinatal care, previable PROM remains a potentially serious complication with important fetal/neonatal implications.

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Cost effectiveness of fullterm fetal fibronectin

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Introduction: Prematurity can have a severe effect on newborns and their families. It also has major implications on the financial resources of the health care system. Fetal fibronectin test can significantly reduce preterm labor admissions, length of stay, and prescriptions for tocolytic agents. Objective: To conduct a pilot study to demonstrate cost savings of Full Term Fetal fibronectin system in UK.

Results: 20 patients were included in the study. The test was negative in 17 patients and positive in 3. For the calculation of cost savings only the patients with negative fibronectin have been included (n=17). 6/17 women received steroids. 4 received tocolysis with Atosiban and 2 with nifedipine. There were no NNU cots in 8/17 cases. Two patients were transferred in utero and 8 patients were admitted for more than 24 hrs. None of these patients delivered within 7 days of the testing. Cost savings were calculated.

Conclusions: This is the first study in UK utilizing the full term system of fibronectin testing and it has demonstrated huge cost savings. This pilot study shows that the use of fetal fibronectin testing will allow rational decisions to be made about patient care in threatened preterm labor. We recommend that inclusion of this testing in hospital protocol will Result in better utilization of our financial resources and manpower, thus leading to improved patient care.

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Transvaginal sonographic assessment of the cervix combined with maternal saliva estriol (E3), cervical fetal fibronectin (fFN) and serum Corticotropin-Releasing Hormone (CRF) for prediction of spontaneous preterm delivery (PD)

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Premature delivery means the termination of pregnancy between its 22 and 37 week. Despite ongoing efforts its incidence hasn’t change for decades and still almost 70% of perinatal mortality and nearly half of neurological impairments originate from preterm delivery. Therefore identification of markers for preterm labor is crucial for proper prophylaxis. The aim of this study was to determine whether the combined, simultaneous sonographic assessment of the cervix and the concentration of: saline estriol, vaginal fFN and serum CRF, IL-6, CRP and cortisol may be useful for prediction of spontaneous preterm delivery. Subjects were 40 patients with spontaneous preterm labor and 37 healthy pregnant women. Patients with spontaneous preterm delivery were examined at the time of admittance to the hospital. In the control group (healthy pregnant women) the measurements were performed at least three times – at 11-14, 20-22 and 30-32 weeks gestation and in 5 of them at the time of delivery. The cervical length and volume was lower in preterm delivery group and corresponded with the fFN. There was a negative correlation between cervical length and fFN. Cervical ultrasound and fFN undeniably have prognostic value in the diagnosis of preterm delivery. Both serum CRF and saliva E3 were associated with a slightly increased risk of preterm birth. Our data suggest that these markers may be helpful in the identification of these patients at risk. Positive correlation between IL-6 and CRP, IL-6 and cortisol levels may be the Result of subclinical infection. This study was supported by grant PBZ-MEiN-8/2/2006.

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Age-related changes of the cervix – sonoelastography during pregnancy

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Introduction: Cervical insufficiency is one of the factors causing premature delivery. Real-time sonoelastography was performed in a normal population versus cervical insufficiency to identify elastic tissue changes in relation to age and week of gestation.

Methods: Fifty-two healthy pregnant women and nineteen patients with cervical insufficiency at a mean of 28 weeks of gestation were examined. In the dual mode, the real-time elastography information was superimposed in color on the B-mode scan (Hitachi). The elastography scans were analyzed by means of a computer program (determination of thresholds for the colors red, blue, and green) and by two independent readers using defined regions of interest (ROIs). The proportion of the elastic color spectrum was determined in relation to the total area of the ROI. The percentages of red and green in the ROI served to calculate an elasticity tissue quotient (TQ). These quotients were correlated with age and week of gestation (ANOVA, Wilcoxon’s test).

Results: The color distribution in the normal population showed that green was predominant (67.1±12.5%) followed by blue (26.5±12.9%) and red (6.4±3.7%). The TQ decreased significantly with increasing age (p=0.026) while tissue elasticity was not affected by the duration of pregnancy (p=0.233). The elastic portions tended to be larger in women with cervical insufficiency as compared with the normal group (78% versus 72%, p>0.05).

Conclusion: The elastography findings did not change with the duration of pregnancy but with the women’s age. An insufficient cervix was found to be “softer” on elastography.

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Invasive fungal infection due to Candida in ELBW newborns

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Invasive fungal infection (ifi) occurs in 10-28% of all ELBW admitted to the NICU. Determination of morbidity rate, clinical and laboratory signs, perinatal, postnatal risk factors and outcome of ifi among ELBW treated in the NICU. Within 5 years 162 ELBW were hospitalized in NICU, among them 27 with 40 episodes of ifi due to Candida. All babies showed clinical signs of infection and had positive mycological cultures. GA<28 of weeks in 78%, BW<700g in 19%, Apgar score <4 in 26% were noted; 81% of them born by caesarean section.

Results. The first signs of ifi were noted <7 day of life in 5% of cases, between 8th and 30th in 20% and 50% all ifi >30 day. Main symptoms included gastrointestinal disorders (45%), pneumonia (38%), renal insufficiency (15%), seizures (10%), shock (10%), hepatosplenomegaly (10%), acidosis (48%), hyponatremia (30%), hypoglycemia (22%), elevated CRP (80%), WBC >20G/l (20%), trombocytopenia (72%). In 26 ELBW mechanical ventilation since birth was necessary, all received antibiotics, TPN and antifungal prophylaxis with intravenous fluconazole, 81% had central venous catheter, 48% were operated. The dominating types of Candida were C.sake (15), C.lusitaniae (11) and albicans (9) sensitive for fluconazole. Positive cultures (blood-9, CSF-5, urine-4, catheter-8, tracheobronchial aspirates-4) were obtained in all newborns. Mortality rate was 30% and mean hospitalization stay was 87.2 days.

No significant correlation between birth asphyxia, RDS, IVH, postnatal risk factors and bad prognosis of ifi in ELBW was shown. Lower BW, GA and higher mortality rate of bacterial sepsis were often noted in ELBW with ifi.

Conclusion. Despite antifungal prophylaxis with fluconazole Candida bloodstream infection is a serious problem among ELBW neonates with high mortality.

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Triplet pregnancies: Management and outcomes

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Objective: To evaluate the management and outcomes of triplet pregnancies.

Setting: Vilnius University Hospital Department of Obstetrics and Gynecology, Lithuania.

Design: Retrospective analysis of all triplet pregnancies managed and delivered in 1996 - 2008.

Results: There were twenty-eight triplet deliveries during the period of 1996 – 2008. The rate of triplets was 0.4:1000 in 2006 and 1.3:1000 in 2008. Assisted reproductive technologies were applied in 16 (57%) pregnancies: 7 pregnancies occurred after treatment with ovulation-induction agents, 8 - IVF and 6 - artificial insemination. The most common complications of pregnancy were premature contractions (n =25; 86%), anemia (n =20; 70%), pregnancy induced hypertension (n =7; 24%), premature rupture of membranes (n =11; 38%). 25 (86%) sets of triplets were delivered by caesarean section, 3 (4%) - vaginally. 96% of triplets were born premature, the mean gestational age was 32.5 weeks±2.6 weeks (range 27-37 weeks). 58 (67%) neonates suffered from respiratory distress syndrome, 20 (23%) newborns were born with hypotrophy, 13 (15%) with hypoxia, 5 were diagnosed with intraventricular hemorrhage. One stillbirth occurred due to umbilical pathology. The causes of 5 newborns' deaths were respiratory distress syndrome, congenital abnormalities and necrotizing enterocolitis.

Conclusions: Rate of triple pregnancies is increasing during last decades with the use of assisted reproductive technologies. Multiple pregnancies are at high risk for severe neonatal morbidity and mortality, mainly due to prematurity and respiratory disorders.

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**Cerebral malformations associated with macrocrania – clinical and paraclinic diagnosis**

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**Objectives:**
Precocious determination of positive diagnosis in the presence of macrocrania, confirmed by the increase of the cranial perimeter with more than 2 percentiles and by the dilation of the ventricular system, visualized with the help of ultrasounds.

**Materials and Methods:**
The study group included eleven premature newborns, which were selected on the basis of clinical and imagistic criteria, hospitalized in the Neonatology Clinic. The cranial ultrasonography was used as a method for diagnosis and the estimation of prognosis. The MRI was used for diagnosis confirmation and determination of the time of the surgical intervention.

**Results:**
The incidence of the cerebral malformations was of 1.24%, the most frequent malformative types being the craniovertebral dysraphisms: -63.63%. Thus the following were associated: Arnold-Chiari type III malformation –18.18%, corpus callosum agenesia – 9.09%, holoprosencephaly – 9.09%. One case presented both meningoencephalocele and the Arnold-Chiari type III malformation.

The clinical signs were the classic ones of hydrocephalia: seizures, paresis, inferior member paralysis, respiratory and cardiac rhythm disturbances.

Cerebral imagistics was utilized for the assessment of ventricular dilatation and the degree of compression of the cerebral tissue.

Although the therapeutic intervention was fast, the ventricular-peritoneal drainage valve was mounted in five cases and the specific anticonvulsive and ethiopathogenic medication was administered, the mortality rate was still high (18.12%).

**Conclusions:**
Rapid-evolving hydrocephalia was the death cause for the associated cerebral malformations. The most frequent malformative types were the craniovertebral dysraphisms, which presented a complete clinical and imagistic picture.

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Hepatobiliar ultrasound and hepatic abscess in very low birth weight infants (VLBWI)

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Background: Hepatic abscess is rare in the neonatal period, if untreated, the outcomes remains uniformly fatal. Major risk factor for hepatic abscess are sepsis, umbilical catheterization, and omphalitis. Minor include NEC, abdominal surgery, maternal infections, infant of diabetic mother, exchange transfusion and asphyxia neonatorum. The signs and symptoms i neoante are non-specific and are essentially those of sepsis. The hepatic abscess can be either multiple or solitary. Routes of infection are: via contagious structure or hepatic artery trought systemic circulation or portal vein via umbilical vein, mesenteric or splenic vein.

Cases Reports: We report 6 cases of preterms with hepatic abscess in the last 5 years. Median gestational age was 30 weeks, birth weight 1,600gr, age of diagnosis was 13.6 days. All babies developed hepatomegalia, abdominal distension, hipertransaminasemia. Staphilococcus, Streptococcus. and E.Coli, Candida, Klebsiella, Pseudomonas were the organism isolated from solitary heaptic abscess in neonates. All infants received antibiotic treatment and amphotericin therapy. Two presents solitary hepatic abscess, dreined by surgical methods, and then treated with appropriate antibiotics. All showed in serial ultrasound hepatobiliar system, the resolution of hepatic abscess.

Discussions: In our babies with major risk factors for epatic abscess we execute ever ultrasound of hepatobiliar system. The diagnosis of liver abscess in these neonates cannot established from the clinical picture alone, is important ultrasound of hepatobiliar or computed tomography, to make early diagnosis.

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Prematurity: Risk Factors and Results for Intraventricular Hemorrhage

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Introduction: Intraventricular hemorrhage is an important cause of brain injury in premature infants. Although, its incidence has declined in the last years, IVH remains a significant problem in premature births.

Objective:
The aim of this study is to show the incidence of IVH in premature infants and to evaluate the risk factors.

Materials and methods: This is a prospective study and there were a total of 415 premature newborns with gestational age less or equal than 36 weeks, hospitalized between January-December 2008 in our hospital. All babies were followed until discharge or death.

Results: The mean gestational age of this population was 31.0±2.2 weeks (min 26 weeks; max 36 weeks) and the mean birth weight was 1,400±350g (min 600g; max 2,000g). IVH was diagnosed in 54 cases (13%). All of babies with IVH had respiratory distress and required resuscitation. As statistically significant risk factors were gestational age, birth weight, apgar score, mother complications, hypotension and sepsis. Maternal corticosteroids administration was found to be significantly protective as well.

Conclusions: As in our country Neonatal Care has its limitations, to prevent IVH is necessary to prevent prematurity, better prenatal care and maternal corticosteroid administration.

Key words: prematurity, IVH, gestational age, birth weight.

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Severe respiratory failure secondary to elective caesarean delivery

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During the past years it was noticed a significant increase in deliveries through caesarean section in the Department of Obstetrics of Clinical Hospital “Dr. D. Popescu” Timisoara (36.5% out of all deliveries in 2008).

In this study it is compared the incidence of respiratory failure in two groups of neonates with gestational age over 36 weeks, born through caesarean section, elective in first group and necessary in the second.

This is a retrospective study over a period of 4 years, between 2005-2008, performed in the Neonatology Department of Clinical Hospital of Obstetrics and Gynecology “Dr. D. Popescu” Timisoara. The study group included 4,104 newborns. The observed respiratory pathology consisted in transient tachypnea, respiratory distress syndrome, persistent pulmonary hypertension, pneumothorax and neonatal death.

The authors conclude that the neonates with gestational age between 36 and 37 weeks born through caesarean section without labor present the highest risk in developing respiratory failure (14.3%) as sign of pulmonary pathology and the risk is decreasing when the delivery is close to term (3.5% in 39 weeks gestational age).

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Pericardial effusion: life threatening complication of central venous catheterization in premature infants (report of 4 survivors at Sousse – Tunisia neonatology department)

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With the increased use of central venous catheters (CVC) in NICU, there have been many case reports of complications. Pericardial effusion (PCE) is a rare but life threatening complication. We report a series of 4 cases of PCE occurring in premature neonates who survived to such a complication.

Respective gestational ages were 27; 30; 31 and 33 GA. Birth weights were 690; 1130; 1200 and 1,900g. Catheterization consisted in jugular internal vein catheterization after surgery in one NN and in umbilical catheterization in 3 NN. Median time from catheter insertion to PCE detection ranged between 5 and 10 days. Sudden respiratory distress was noted in 2 neonates whereas the 2 others were suddenly shocked. Catheter tip was in the right atrium in all cases. PCE diagnosis was confirmed with echocardiography in 2 cases and thoracic ultrasounds in 2 cases. Pericardial drainage was performed in 3 NN and pericardiocentesis in one NN presenting with signs of tamponade. Total remove of the catheter was indicated in all cases. Rapid improvement was noted in all NN.

27 W NN died 1 month after this complication due to a severe sepsis.

PCE complicating CVC, although rare, is a severe condition. It is generally in relation with a right atrium tip CVC placement. In any infant with a CVC in situ who deteriorates suddenly, PCE or cardiac tamponade must be considered and appropriate action taken emergently. Prognosis is related to rapid diagnosis and treatment that has to be started in the NICU.

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The investigation of the role of plasminogen activator inhibitor-1 4G/5G gene polymorphism in bronchopulmonary dysplasia

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Activation of the coagulation cascade leads to intraalveolar fibrin deposition in many inflammatory pulmonary disorders. Proinflammatory cytokines activate coagulation via tissue factor and attenuate fibrinolysis by increasing the level of plasminogen activator inhibitors. Bronchopulmonary dysplasia (BPD) continues to be one of the important causes of morbidity and mortality in preterm neonates. Different individual factors may have role in the pathogenesis of BPD among preterm infants. Plasminogen activator inhibitor-1 is one of the genetic factors that may have a role in the pathogenesis of the disease. We investigated the role of plasminogen activator inhibitor (PAI)-1 4G/5G gene polymorphism in BPD. The study group comprised of 98 preterm infants with BPD and control group included 94 preterm infants without BPD. The neonates with congenital anomalies and the neonates who died during the first 28 days of life were excluded from the study. We analyzed PAI-1 4G/5G gene polymorphism by polymerase chain reaction and restriction enzyme digestion (RFLP). Preterm infants were divided into three groups according to their genotype including 4G/4G, 4G/5G and 5G/5G. Of the BPD group, 43.9% had 4G/4G (n=43), 27.6% the 4G/5G (n=27) and 28.6% had 5G/5G (n=28) genotype. On the other hand, control group 42.6% had 4G/4G (n=40), 28.7% had 4G/5G (n=27) and 28.7% had 5G/5G (n=27) genotype. There was no statistically significant difference between two groups.

In conclusion, we could not show any association between PAI-1 4G/5G gene polymorphism and BPD in our study group.

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Glutathione-S-transferase-P1 (GST-P1) polymorphism is not associated with bronchopulmonary dysplasia in low birth weight preterm infants in a Greek population

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Background: Bronchopulmonary dysplasia (BPD) is a common perinatal complication of premature infants with a significant risk of long-term disability and morbidity. Many factors have been implicated in BPD pathogenesis, with oxidative stress being one of them. In a previous African American study, genetic variations in the GTP-1 gene have been significantly associated with BPD, suggesting a possible role of detoxification enzymes, such as GST-P in the development of BPD.

Objective: The purpose of this prospective was to examine the association between the GST-P1 val105ile polymorphism and BPD, in an independent Greek cohort of BPD cases and controls.

Methods: Our study group was composed of 61 premature infants, of whom 28 had BPD, and 41 controls. PCR and RFLP methods were used for the genotyping of the GST-P1 val105ile polymorphism. Comparison of genotype frequency distributions in BPD cases and controls was done with the $\chi^2$ test of independence. Results: The distribution of genotype frequencies was ile/ile=73.68%, val/ile=18.42%, val/val=7.89% and ile/ile=78.05%, val/ile=19.51%, val/val=2.44% for the BPD cases and controls, respectively (P=0.54). In the subgroups of BPD and non-BPD premature infants the GST-P1 genotype frequencies did not reach statistical significance, as well (P=0.86).

Conclusion: Our Results on the distribution of GST-P1 genotypes show no difference in GST-P1 genotype frequencies between BPD cases and controls, thus GST-P1 does not seem to have a crucial disease causing role. However, the genetic contribution of this gene in BPD needs to be studied in different ethnicities.

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Minute endogenous exhaled nitric oxide and endotracheal nitrites-nitrates in the mechanically ventilated preterm newborn. Relation with chorioamnionitis and bronchopulmonary dysplasia


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Study objective: To analyze the evolutive changes of the early exhaled NO (eNO) and nitrites-nitrates (NOx) in mechanically ventilated preterm newborns, according to history of maternal chorioamnionitis or appearance of bronchopulmonary dysplasia.

Patients: Preterm newborns mechanically ventilated in the first 60 hours after birth.

Method: Observational study of intubated preterm infants. Collection of a sample of endotracheal air exhaled during 3 minutes is performed to measure NO (by NOA Sievers machine) during aspiration time. Meanwhile, ventilatory characteristics are recorded to obtain minute ventilation volume without leaking. Endotracheal secretions to determine NOx are collected at the end of the procedure. Results are compared according to chorioamnionitis history or bronchopulmonary dysplasia appearance and normalized applying an experimental formula.

Results: 46 ventilated preterm infants (14 with chorioamnionitis and 32 without it) have been studied. There was no environmental contamination. Chorioamnionitis group had less gestational age and caesarean section rate, and their newborns showed more patent ductus arteriosus and severe intraventricular hemorrhage. They presented higher eNO/minute/kg (0.42 vs. 0.29, p=0.040) and higher normalized eNO/minute/kg (1.54 vs. 0.90, p=0.016). eNO/minute/kg was related to endotracheal NOx (r=0.386, p=0.038) and normalized eNO/minute/kg seems a good predictor of bronchopulmonary dysplasia (area under curve of 0.864; p=0.002).

Conclusions: Chorioamnionitis increases eNO/minute/kg as well as normalized eNO/minute/kg in mechanically ventilated preterm newborns.

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The combined use of fetal Fibronectin and transvaginal cervical length for assessing the risk of preterm birth

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Objectives: To assess the combined use of cervical length (CL) and cervicovaginal fetal fibronectin (fFN) in women with threatened preterm labor.

Methods: Patients with singleton pregnancies and regular uterine contractions between 23+0 and 33+6 gestational weeks were included. FFN samples were collected at the time of speculum examination from the posterior cervical fornix. Results were blinded to the managing obstetrician. The probe was analyzed using the Rapid Fetal Fibronectin TLI System. CL was measured afterwards by transvaginal ultrasound. A CL ≤ 25 mm was an indication for admission and treatment. Outcome data were collected after delivery.

Results: 125 patients with singleton pregnancies were tested for fFN (mean gestational age at admission was 29 weeks; at delivery 38 weeks).

99 had a negative fFN result. 26 a positive test result. Of those 81 pts are already delivered. 22pts were fFN pos (27%). 10 were delivered < 35 weeks (45%), 7 < 38 weeks (32%) and 5 ≥ 38 weeks (23%). Although 6pts had a CL > 20 mm 4 were delivered < 38 weeks.

In FFN pos patients with a CL 16-20 mm (n=5) 1 was delivered < 35 weeks and < 14 days; CL 11-15 mm (n=2) 1 within 7 days and 1 within 14 days and CL ≤ 10 mm (n=9) 2 pts were delivered within 48 hours, 4 within 7 days and 4 within 14 days. 59 patients were fFN neg (73%). 2 were delivered < 35 weeks (3%), 10 < 38 weeks (17%) and 47 ≥ 38 weeks (80%).

FFN neg patients with a CL > 20 mm (n=36) were neither delivered within 7 days nor < 35 weeks (3 pts < 38 weeks), CL > 15 ≤ 20 mm (n=5) none within 14 days, 1 < 38 weeks, CL > 10 ≤ 15 mm (n=10) 1 was delivered within 14 days, 2 < 35 weeks, 2 < 38 weeks and 6 > 38 weeks.

None of the pts with fFN neg and a CL ≤ 10 mm (n=8) were delivered within 14 days or < 35 weeks.

Conclusion: The combination of CL and FFN shows a high neg predictive value and a high sensitivity. Patients who were delivered < 35 weeks were either fFN pos or had a CL ≤ 15 mm.

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Risk assessment for early and very early preterm birth – a retrospective cohort study

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Aim: To examine the relationship between preterm delivery, with a focus on early and very early preterm delivery, and risk factors both in the obstetric history as well as social and medical factors of the current pregnancy. Identifying women at risk of early and very early preterm delivery offers a chance of prevention.

Material and methods: We analyzed data from the perinatal statistics of eight German federal states of 1998-2000; n=508,926 singleton pregnancies. We compared risks of pregnancy and birth between preterm and term births. We sub-divided preterm delivery into very early preterm delivery (<28 weeks’ gestation, n=1,910), early preterm delivery (28-31 weeks’ gestation, n=3,425), and moderately early preterm delivery (32-36 weeks’ gestation, n=27,267).

Results: The overall preterm birth rate (≤36 weeks gestation) was 6.5%. Psychological stress was noted in 4.6% of women experiencing very early preterm birth but only in 2.7% of women having a term birth. Pregnancies that ended with very early preterm birth commonly occurred in women who had experienced two or more previous miscarriages or terminations (n=324, 17.0%), bleeds before 28 weeks’ gestation, (n=364, 19.1%), cervical incompetence (n=311; 16.3%), and premature labor (n=637, 33.4%).

Conclusions: Prevention of early preterm delivery should include screening for risk factors associated with early preterm delivery, early detection and treatment of vaginal infection (vaginal dysbiosis) to avoid premature rupture of membranes, and restoring vaginal flora after local anti-infective treatment. The validity of “home uterine monitoring” in high risk groups has not yet been proven.

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Fetal abdominal cysts: Prenatal detection in the first trimester and postpartal correlation

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No Abstract attached!

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Objective: Ultrasound has become a widespread noninvasive method for prenatal screening and diagnosis. In our retrospective study we determined the accuracy of ultrasonography in screening for fetal malformations.

Methods: the study was performed over a period of 7 years (2000 – 2006) and we focused our research on 1311 major or minor relevant malformations. In most of the cases, the prenatal diagnosis of malformation was established on ultrasound criteria.

Results: the most frequent fetal anomalies detected in our clinic were: chromosomal anomalies (trisomy 21 – Down syndrome, trisomy 13 – Patau Syndrome, trisomy 18 – Edwards syndrome, Turner syndrome, cri du chat syndrome); central nervous system malformations, especially neural tube defect – spina bifida, anencephaly, encephaloceles; cardiovascular malformations; anomalies involving the renal and urinary tract system, the abdominal wall and digestive system, the face and the limbs. Ultrasound sensitivity for major abnormalities was 94.3% and for minor abnormalities 43.6%.

Conclusions: routine ultrasound examination can achieve a detection rate of congenital anomalies. Apart from the diagnosis of cardiac abnormalities, the Results are satisfactory and justify routine ultrasound screening for malformation. It is expected that ultrasound will continue to improve, and it is hoped that techniques used in the fields of noninvasive prenatal diagnosis will continue to advance.

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Autoaudit on the ultrasound prenatal diagnosis in a local hospital

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Introduction: The increase of demands and the importance of the prenatal diagnosis shows us that the ultrasonography assessment have capital importance in our daily practice, therefore the qualification degree is fundamental.

Objective: To determine the effectiveness of the ultrasound prenatal diagnosis in our service.

Material and methods: We analyzed the major fetal anomalies occurred from 2005 to 2008 in our hospital with monitoring in the pregnancy office and established the correlation with the prenatal diagnosis. In order to measure the effectiveness we determined sensitivity, specificity and predictive values.

Results: We had 28 congenital malformations of a total of 2,160 gestations controlled during the studied period (1.3%). 20 were diagnosed correctly, another 8 malformations were undiagnosed (corresponding 7 to nonsevere congenital heart defects: CIA-CIV and a case of hypoplasia of the forearm) and in 3 occasions with a diagnosis of malformation, it was not confirmed later. We obtain a sensitivity of 71.4%, specificity 99.9%, positive predictive value 87% and negative predictive value 99.6%.

Conclusions: Although in the ultrasound prenatal diagnosis we must demand ourselves high standards to quality, we thought that we reached an optimal effectiveness in the detection of malformations after this autoaudit. On the other hand to review that the sonography heart assessment constitutes a major goal because of the importance of a correct diagnosis of congenital heart defects and in our plan of training we must improve this technique.

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Sonographic diagnosis of holoprosencephaly in the first and second trimester

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Holoprosencephaly (HPE) is a developmental abnormality of the fetal brain, resulting from failure of cleavages of the prosencephalon. The incidence is about to 6-12:10,000 among live born but 1:250 in embryos. The etiology of holoprosencephaly is heterogeneous and not completely known. Approximately 30% of all affected have an underlying chromosomal disorder. The prenatal sonographic diagnosis of alobar holoprosencephaly was first described in 1984.

We report three patients with alobar holoprosencephaly, one a fetus at 24th week of gestation and two cases in the first trimester.

The fetuses in the first trimester had a crown-rump length of 48mm and 56mm. Transverse sonogram demonstrated a monoventricule and fused thalami. The principal sign (« butterfly sign ») were absent. Facial dysmorphia hypotelorism was associated. 4D ultrasound confirmed the malformations seen on the 2D scan. No other malformation could be seen. The pregnancies were terminated.

Sonogram of the fetus at 24th week demonstrated a monovetricule and fuse thalami, proboscis above the fused eye and midfacial hypoplasia.

Prenatal diagnosis of HPE long time was performed in the second trimester. With increasing quality of ultrasound equipment detection of HPE is now possible at an earlier gestational age. Failure to identify the butterfly sign is a warning sign of holoprosencephaly in the first trimester. Systematic identification of the butterfly sign at the time of sonographic assessment of nuchal translucency provides a valuable tool for the early screening of holoprosencephaly. An early diagnosis allows an easier pregnancy termination, when such severe anomalies are found.

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Frontoparietal encephalocele linked with aneuploidy – case report

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The incidence of encephalocele is about 1-4 per 10,000 live births. While the occipital encephalocele is the most common form of encephalocele in the Western Hemisphere, the most common type of encephalocele in Southeast Asia is frontoparietal. The prognosis depend on the site, size, and contents of the encephalocele. The ultimate outcome depends on the patient's karyotype and associated syndromes, as well as on the ease of surgical correction. A good prognosis is indicated for a patient who has an anterior encephalocele containing no brain tissue and who has no associated anomalies. Poor prognostic indicators include a large or posterior encephalocele and systemic anomalies.

Case report: A woman 21 years old G2P1A0, presented in 16th week of gestation with encephalocele in frontoparietal region and hyperechogenic bowels noted on ultrasound exam. In order to consider possible chromosome disorder, during procedure of therapeutic pregnancy termination, we sent amniotic fluid sample to cytogenetic examination, which revealed Trisomy 21.

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Agenesis of the corpus callosum and genetic mechanisms involved

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Agenesis of the corpus callosum (ACC) is among the most frequent human brain malformations with an incidence of 0.5-70 in 10,000 and is considered to be a component of as many as 50 to 200 different syndromes. Genetic factors are probably predominant. Ultrasound diagnosis of ACC is possible from midgestation onward but it is a difficult one, especially of the partial type of ACC. When ACC is an isolated finding it is associated with a normal to borderline intellectual development in most cases.

We present the case of 29-year old woman admitted at 30 weeks of gestation with vertex presentation for ultrasound examination. Transverse axial plane revealed teardrop-like shape of lateral ventricles measuring 9.4mm and respectively 9.6mm and the absence of cavum septi pellucidi. Sagittal plane obtained by vaginal sonography revealed the absence of the posterior portion of the corpus callosum and an abnormal branching of the anterior cerebral artery that had been demonstrated with the use of color Doppler ultrasound. No other fetal structural anomalies had been found and we established the diagnosis of isolated partial ACC. The diagnosis was confirmed after birth by transfontanellar ultrasound examination and MRI and molecular genetic testing were performed. We review other published cases and discuss the postnatal outcome and genetic factors potential etiologically involved that could influence the development of compensatory mechanisms.

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Intraventricular hemorrhage in term newborn – case report

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The aim of this research is presenting neurological outcome in full-term newborn born at Clinic for Gynecology and Obstetrition in Nis which has been diagnosed having IV grade IVH. The baby is from controlled pregnancy. In 9th month of gestation mother has had respiratory infection with febrile state. Delivery was in term, finished by vacuum extraction. Male newborn with BW 4150g / 59cm, Apgar score in the 1st minute was 8. The baby had respiratory distress, and clinical findings included fever, seizures, full fontanel and irritability.

The child was examined neurologically, ultrasonographically in first week of life and monthly until the first year ended, also using MRI and CT scans, as well as EEG. CNS ultrasonography showed IVH of the IV grade. MRI scan in the 30th day of life has shown both-sided frontoparietal leucomalation; spot-like deposition in the white matter of the both frontal regions periventriculary; compensatory ventricular dilatation; discrete posthemorrhagic changes in both thalamic regions; left-sided subependimal cystic lesion. Ultrasonographically, in two months of life, there was not a progression of ventricular dilatation. In 2nd month of life, habilitation program has started. Developmental milestones have been accepted from the schedule for the age. In 10th month of life EEG shows specific epileptiform changes.

Associated damages and regenerative potential of brain tissue are most important for long-term prognosis. Psychomotoric development of the reported child in the 30th month of life is normal, but longer follow-up studies are needed until school age to see whether these infants develop other neurological impairments.

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Cranial ultrasound abnormalities in premature infants (<1,500g) and neurodevelopmental outcome

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Objectives: To describe the correlation between Cranial Ultrasound (CUS) findings in preterm and their neurodevelopmental outcome at 2 years corrected age.

Subjects and Method.- A sample of 1184 preterm infants born from 1996 to 2006. Gestational age distribution was ≤28 w, 32.1%; 29-30 w, 30.6%; ≥31w, 36.7% and weight rates: 500-749, 11.9%; 750-1000g, 22.1%; and 1001-1500g, 64.9%. Neurodevelopmental outcome was assessed by structured neurologic examination. At 24 months a psychometric evaluation was made.

Results: CUS was performed in 1131 (95.5%) cases, (53 were not done for early death -28 in first day-), and was normal in 877 (76%). Abnormal findings in 249 infants included intraventricular haemorrhage (IVH) 168 (67.5%), periventricular leukomalacia (PVLM+ cystic lesions) 52 (20.8%), Hypoxic Ischaemic lesions 5 (2%), Parenchymal Haemorrhage 17 (6.8%), Subarachnoidal Haemorrhage 4 (1.6%), Subdural/Epidural Haemorrhage 1 (0.4%). 2 cases died and 137 were lost (14.6%) during follow-up. Mortality in infants with normal CUS/HIV I/HIV II was 10.7% vs. 74% in IVH 3-4 group (p=.000). PVLM was not of significant value for survival (85.6 vs. 76.9%; p=0.06). In survivors the follow up shows a major neurological disability in ≤25w group (24%) vs. >26-31 w group (5-6%), but increases in 34-36 w group to 7%, probably due high rate of patients with IUGR. Conclusions: CUS is an available and easy tool for imaging neonatal brain. IVH and PVLM are independent predictors to neurological disability in follow up. [IVH 3 4 (OR 4.6) and PVLM (OR 5.3)].
Fetal akinesia deformation sequence – case report

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Fetal akinesia deformation sequence (FADS) is a rare condition characterized by intrauterine growth restriction, congenital limb contractures, pulmonary hypoplasia, hydramnios and craniofacial abnormalities. Prognosis is generally poor and medical termination of pregnancy is proposed. The authors present 2 clinical cases in which FADS was suspected. First case was a 20 year-old-woman, G1P0, that at 13 weeks sonography revealed an increased nuchal translucency thickness (NT) and nasal bones present. At 18 weeks the sonography disclosed fetal anasarca, absence of fetal movements (FM) and hydrops fetalis. The serologic tests were normal. The patient was submitted to amniocentesis (at 14 weeks) revealed FISH 13(2); 18(2); 21(2); XX. She decided for medical termination of pregnancy. The second case was a 26 year-old-woman, G2P0, that sonography at 13 weeks showed increased NT, cystic higrome, present nasal bones, normal doppler fluxometry. At 16 weeks she performed an amniocentesis that revealed normal karyotype, 46,XX. The sonography at 18 weeks demonstrated lack of FM, fetal hydrops, deformation of the feet, fixed flexion deformity of the hands, retrognatia and no visualization of the stomach. Fetal cardiac sonography detected pleural effusion. Maternal infection screening was normal. Pregnancy was terminated at 22 weeks. External examination showed a female fetus with marked muscular hypoplasia, fixed flexion of lower and upper limbs, bilateral clubfoot and cervical edema. The autopsy confirmed prenatal sonographic suspicion of arthrogryposis. Molecular, neuromuscular, enzymatic and cytochemical screening were normal. These 2 cases demonstrate the importance of early sonographic screening of fetal anomalies in particularly increased NT in early diagnosis of FADS.

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Fetal seizures as a prenatal marker of congenital metabolic disease

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We report a rare case of fetal seizures, on the third trimester of gestation, diagnosed by ultrasound and secondary to a congenital metabolic disease. Unlike other published cases of fetal seizure activity, there were no malformations associated.

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Prenatal diagnosis of aorto-pulmonary window, double-outlet right ventricle, and absent pulmonary valve: A case report of immediate neonatal death

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A congenital heart disease with a combination of aorto-pulmonary window (APW), double-outlet right ventricle (DORV), and absent pulmonary valve (APV) is extremely rare and has not been reported elsewhere. Here we report a prenatal diagnosis and perinatal course of a fetus with this combination. A 27-year-old woman, gravida 1, para 1, was referred to our institute at 27 weeks of gestation for the assessment of the cardiac anomalies. Detailed ultrasonography (US) of the fetus revealed a complex cardiac anomalies of a large A-P window, DORV, APV, and ventricular septal defect (VSD). The fetus had no other abnormal findings such as hydropic change, structural anomalies in other organs, and polyhydramnios.

The clinical course of the mother and the fetus was uneventful thereafter, and the induction of labor was scheduled at 39 weeks. The baby girl, 3,280gr, was born after 8 hrs of induction with oxytocin. In spite of no deteriorating fetal heart rate pattern during labor, the baby had cardiac arrest at birth with Apgar 0(1') and 1(5'), and she died 30 min after birth without any reaction to intensive resuscitation. The autopsy confirmed the prenatal diagnosis with no other anomalies. The baby did not have any abnormal findings in the respiratory tract and the pathogenesis of the sudden neonatal death was not proved.

A further accumulation of case reports of similar cases would be informative in the future for the management of the baby with this cardiac anomalies and the explanation to the patient’s family.

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**Complex fetal cardiac defect – pregnancy management – case report**

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The four-chamber view is an effective screening tool with a sensitivity of 40% to 50% for detecting congenital heart disease. The use of multiple cardiac views can increase the prenatal detection. The fact is that most infants with congenital heart disease are born to low-risk women and routine screening is warranted. Early prenatal diagnosis provides an opportunity to exclude associated extracardiac and chromosomal abnormalities, discuss pregnancy options, adjust obstetric management, prepare parents for delivery of an affected baby in a tertiary care center. Despite the widespread use of ultrasonography, only 15% to 30% of infants with congenital heart disease are identified prenatally.

Case report: A woman 23 years old, G1P0A0, presented in 28th week of gestation with complex fetal heart defect, revealed by sonographic examination: atresio v.tricuspidalis, VSD, ASD and aortic coarctation. No other disorders were detected by ultrasound. Because of bad prognosis, we decided for therapeutic termination of pregnancy. We analyzed kariotype from fetal blood sample and no chromosome disorders found.

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Right aortic arch with vascular ring diagnosed at 21 weeks of gestation by three-dimensional ultrasound

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Isolated right aortic arch is a rare congenital heart malformation with reported incidence of about 1 in 1000 low-risk pregnancies. We present a case of isolated right aortic arch which was diagnosed at 21 weeks of gestation during a routine fetal morphological survey. The clue for the prenatal diagnosis was the presence of the so-called U-sign – formed by the vascular entrapment of the trachea and esophagus between the right aortic arch and the left ductus arteriosus. The prenatal sonographic findings were confirmed after birth.

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Congenital cytomegalovirus infection (CMV) and coronary arteries abnormalities: 
Two cases reports

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Although 90% of congenital CMV infections are clinically asymptomatic at birth, 10% of infected infants manifest neurological and neurosensorial involvement. CMV has been implicated as a possible cause of endothelial vascular damage, leading to vasculitis or thrombosis. In literature has been described a neonatal case of aortic arch thrombosis. We report two cases of coronary arteries abnormalities as a Result of congenital CMV infection. A full term infant, manifested clinical signs of systemic CMV infection: hearing loss, DIC, blindness, intracranial calcifications. Echocardiogram showed left ventricular dilatation, reduction of SF (22%) and remarkable increase echogenicity of coronary arteries. During antiviral treatment they returned to normal image with recovery of heart function. A male full term infant who manifested moderate RDS. Also in this case echocardiogram revealed dilated coronary arteries with important increased echogenicity. Laboratory studies showed abnormal levels of BNP, CK, CK-MB. On the basis of the previous case, these data were considered evocative for CMV infection, confirmed by laboratory exams. After 2 weeks the echocardiogram showed a normalization of coronary arteries dilation with a later, progressive decrease in hyperechogenicity.

Kawasaki disease is the most important vasculitis involving coronary arteries, and it is very rare in newborns. On the basis of our experience, it would be reasonable, in presence of increase coronary arteries echogenicity, to investigate for a possible congenital CMV infection. It will be estimated, also in the light of others new reports, the necessity to include echocardiography in the assessment of congenital CMV infection.

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Linear tranducer value estimation in Down’s syndrome screening in the first trimester of pregnancy

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Introduction: Nuchal translucency (NT), nasal bones (NB) and fronto-maxillary facial (FMF) angle are sonographic markers of increased risk for Down’s syndrome in the first trimester of pregnancy.

Objective: The aim of this study was to estimate the quality of these markers obtained by different transducers.

Patients and methodology of investigation: Throughout the period of four years we performed examinations in 320 patients in the first trimester of pregnancy (11-13 6/7 GW) on HDI 5000 using convex transducers (C7-4MHz and C5-2MHz), vaginal (8-4MHz) as well as linear one (L12-5MHz). Main criteria were: 1. sharpness of linear cervical structures for NT, 2. both nasal bones in sagital and transverse plane section for NB, 3. “two lines” belonging to mouth roof/maxilla border on sagital fetal head section for FMF angle.

Results: The quality of all these markers was better in 60% of patients by use of linear transducer. Furthermore, this comparative superiority was evident for structures assessed in distance up to 6cm, while vaginal transducer was more reliable for more distant elements. Linear transducer enabled optimal assessment of all markers in almost 80% of patients, while structures in the remained 20% needed to be further evaluated either by vaginal, or, rarely, convex transducer.

Conclusion: During the first trimester of pregnancy the best quality of sonographic markers in Down’s syndrome screening was obtained in majority of patients by use of linear followed by vaginal transducer. Visualization of these markers was significantly less reliable by convex transducers.

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Sonographic demonstration of hypoplasia of the middle phalanx of the fifth digit: A finding associated with Down syndrome - one case report

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Introduction: Down syndrome is the most common human disease caused by a structural chromosome defect. The incidence is 1 in 800 to 1,000 newborns. The risk increases with maternal age. There are several types of screening test for Down syndrome. Approximately 90% of Down syndrome cases are detected during first-trimester screening by combining maternal biochemistry and nuchal translucency measure. In addition, some ultrasonographic findings for Down syndrome was described, and it also helpful for detecting Down syndrome. In 2010, we report a case of Down syndrome with nasal bone length 3.81mm and hypoplasia of middle phalanx of fifth digit. On the basis of these ultrasonographic findings, termination of pregnancy was offered.

Case report: A 37 year-old, gravida 3, para 2, female patient presented to our outpatient clinic for regular antenatal care. Her first two pregnancies were uneventful, and the two babies were healthy. Antenatal ultrasonography revealed nuchal translucency thickness measured 3.57mm at the 12th week of gestation. Amniocentesis was performed at 16 weeks’ gestation, and it revealed an abnormal female karyotype with trisomy 21, consistent with Down syndrome. Then ultrasonographic investigation was performed at 17 weeks’ gestation, and it showed nasal bone length 3.81mm, ventricular septum defect and hypoplasia of middle phalanx of fifth digit. On the basis of these ultrasonographic findings, termination of pregnancy was offered.

Discussion: Ultrasonographic findings for Down syndrome are cardiac defects, duodenal atresia, hydrops, nuchal thickening, hyperechoic bowel, pyel ectasis, shortened limbs, and hypoplastic or absent nasal bone. It has been established that 60% of infants with Down’s syndrome have hypoplasia of the middle phalanx of the fifth digit. Ultrasound visualization of the middle phalanx of the fifth digit gradually increases during the 13- to 17-week period. These findings confirm the presence of a small middle phalanx in fetuses with trisomy 21 as early as 15 to 16 weeks and may be a useful adjunct to the several already reported sonographic signs in the fetus at risk for Down's syndrome.
Linear transducer reliability estimation for fetal heart morphology and Down's risk assessment in the first trimester of pregnancy

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Introduction: Fetal heart morphology is confirmed to be an important ultrasound marker for Down’s syndrome increased risk in the first trimester of pregnancy.

Objective: In order to estimate the best quality of scan obtained and the transducer used, we assessed fetal heart structures by convex, vaginal and linear transducers obtaining four-chamber heart section, LVOT & RVOT and their relationship on 3VV (three vessels plain section), aortic and ductal arch.

Patients and methodology of investigation: This study was carried out during the period of four years, and involved 320 patients examined in the first trimester of pregnancy (11-13 6/7 GW) on HDI 5000 using convex transducers (C7-4MHz and C5-2MHz), vaginal (8-4MHz) as well as linear one (L12-5MHz). Fetal heart was evaluated using appropriate software with color Doppler, SONO CT and XRES technology. Ultrasonography was performed according to the standardized protocol by especially trained three ultrasonographers. All images were scored by a single reviewer, and feedback was provided to other two doctors.

Results: In 90% of patients linear transducer was better than convex one for fetal heart morphology scan quality assessment on distances up to 6cm from the transducer, while in 80% of patients more distant structures were more reliably evaluated using vaginal than convex probes.

Conclusion: The best quality of fetal heart morphology was achieved in the vast majority of patients by use of linear transducer for structures up to 6cm, while vaginal one was found to be more reliable for more distant elements than convex transducers.

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Congenital diaphragmatic hernia: Prenatal diagnoses and outcome

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Congenital diaphragmatic hernia (CDH) occurs sporadically with an incidence of 1–2/5000 of newborns, depending on whether stillbirths are included or not. CDH does not designate one single clinical entity. CDH outcomes are diverse and contribute significantly to perinatal morbidity and mortality.

Objective: Review of cases of prenatally diagnosed congenital diaphragmatic hernias with special regard to time of diagnosis, organs herniated into the thorax, associated malformations, and outcomes.


Results: The medium diagnosis age was 21 gestational weeks. The diaphragmatic defect was in the left side in 7 cases. The liver was intrathoracic in 2 cases. Three fetus had major malformations. Amniocentesis revealed an abnormal cariotype in 2 cases. The 1st trimester ultrasound was performed in all cases and none had abnormal nuchal translucency. Medical interruption of pregnancy was performed in three cases, because of associated malformations. In 2 cases perinatal dead occurred; in both there were cardiac abnormalities and intrathoracic liver. When the diagnosis was made before 20 weeks of gestational age, mortality was 100%.

Conclusion: Prenatal diagnosis of CDH allows timely referral to a center for perinatal care with multidisciplinary team in the areas of Obstetrics, Neonatology and Pediatric Surgery. The prognostic assessment and the outcome are highly variable.

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4D examinations of the fetal behavior: Where are we now?

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4D ultrasonography made the revolution in examination of fetal neurological development. The most important examinations are the examinations of fetal cardinal movements-CFM and they are measure for the fetal neurological maturation. The goal of this study is to detect the groups with different fetal behavior in the presence of the chronic diseases in pregnancy or to detect the presence of neurological failure in correlation with it. Fetal behavior in the first trimester: first reflex is the grasp reflex detected in 11.4 weeks, breathing suckling, fetal generalized movements. In the second trimester grasp reflex is present with the same incidence like in the first trimester. Movements: cardinal movements and fetal facial expressions. In the third trimester we analyzed fetal facial expressions.

Methodology: Two groups: group A 50 physiological pregnancies 28-40 weeks gestation and group B 50 pregnancies with pPROM, diabetes mellitus, epilepsy in each group 12 pregnancies). We examined fetal reflexes, CFM, fetal facial expressions, and analyze the differences.

Results:
Epilepsy-in the first trimester fetal movements occurred later for each movement the 7.4 days. In the third trimester we found the facial expressions and CFM with higher incidence in the patients on two antiepileptic drugs. In the group with diabetes mellitus we found the higher incidence of CFM, fetal and respiratory movements.

Discussion and conclusion: In the group with PPROM we have the 2 cases of cerebral palsy. Chronic fetal hypoxia in the cases of oligoamnions and infections could be the cause of cerebral palsy, but in these cases we found no ultrasound markers for the antenatal diagnosis.

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Ultrasound characterisation of fetal bowel and neonatal outcome of gastroschisis

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Objective: The aim of the study was to evaluate the usefulness of prenatal sonographic parameters to predict neonatal outcome of gastroschisis.

Methods: Ultrasound findings of fetuses with gastroschisis over a 7 year period (2001-2008) were reviewed. Various sonographic parameters assessed included: bowel diameter, wall thickness and grey-scale analysis of the bowel. The fetuses were divided in two groups, based on the presence or absence of intestinal complications after delivery.

Results: 30 patients met the entry criteria during the study period. 15 neonates have bowel complications in form of intestinal atresia, perforation, presence of necrotic segments, microcolon and volvolus. In 15 cases (50%) pathological ultrasound findings were the indication for caesarean section. Other indications were preterm labor, rupture of membrane, and intrauterine growth restriction with pathological fetal heart rate. In the first group 5 neonates (33%) have intestinal complications, respectively 10 (66%) in the second group. The bowel lumen was significantly larger in the group with complications. The wall thickness and the relationship between diameter to wall thickness showed no correlation only trends. Grey-level histogramm width was higher in the group with complications.

Conclusion: Ultrasound characterization of fetal bowel with grey level histogramm width together with bowel wall thickness and diameter can help to identify severe bowel problems in fetuses.

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Management of a complicated case of gastroschisis

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Gastroschisis is a congenital malformation characterized by an abdominal wall defect located laterally to a normal umbilicus that results in the evisceration of abdominal contents. The cause is unknown but most authors consider it exogenous, such as the maternal use of aspirin, oral contraceptive, cocaine, alcohol, cigarettes and malnutrition added to the younger maternal age. A 25-year-old primipara was referred to our high risk pregnancy unit because of a diagnosis of fetal gastroschisis at 16 weeks’ gestation. No exogenous causes were found, no family history of abdominal wall defects or any other malformations were referred. The fetus presented a 3cm abdominal wall defect located to right side of the umbilicus and a large portion of the bowel protruding, not covered by membrane. Amniocentesis showed a normal fetal karyotype (46,XX). A careful ultrasonographic assessment and a magnetic resonance were undertaken to exclude associated structural anomalies. At 31 weeks’ gestation a complication consisting in a bowel obstruction associated to altered fetal Doppler Velocimetry was seen during a sonographic examination. An emergency caesarean section was undertaken followed by an uncomplicated surgery. The infant stayed in neonatal unit for 5 weeks and after 25 days from the operation he started gradually enteral nutrition. At discharge the baby was in good general condition. A multidisciplinary approach with obstetricians, neonatologists, paediatric surgeons and, most of all, a very close prenatal ultrasound surveillance may prevent severe bowel loss and postnatal mortality (with a tempestive caesarean section and a postnatal surgery intervention).

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Omphalocoele – pregnancy course and outcome – case report

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The outcome of fetus with abdominal wall defect is significantly affected by the presence of additional structural or chromosomal malformations; appropriate multidisciplinary counseling and management is necessary. In cases without associated multiple severe abnormalities, the perinatal outcome could be favorable. There is no convincing evidence to support routine caesarean section for most abdominal wall defects.

Case report: A woman 27 years old G1P0A0 presented in 17th week of gestation with anterior fetal abdominal wall defect – omphalocele. In order to investigate possible related DNA disorders, we performed amniocentesis which revealed normal karyotype. Pregnancy continued till term and vaginal birth occurred: live male newborn 4,390g, Apgar score 7/8, with associated hypospadia, transferred to Neonatal care unit to imminent treatment.

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Early prenatal ultrasound diagnosis omphalocele of edwards syndrome – a case report

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Introduction: Edwards syndrome or trisomy 18 chromosome appears to be the second most common of the autosomal trisomy syndromes, with an incidence between 1:3500 and 1: 8000 live birth. Present case: We present the case of prenatal diagnosed Edwards syndrome during first trimester pregnancy. The woman was aged 26 years, with no positive hereditary anamnesis. Ultrasound screening showed nuchal translucency of 3mm deformity of the fetal abdominal wall was observed, dimensions of 19.5x22mm, indicating omphalocela, which was the main indication for early amniocentesis and karyotyping. Karyotyping from amniotic fluid, performed in 14+3 gestation week, revealed aberrant female karyotype 47,XX,+18- Syndrome Edwards. In the second ultrasound control, when karyotyping was finished, significant enhancement of omphalocela was observed (34mmx32mm), where of all visceral and abdominal organs were there. Moreover, discontinuity of ventricular septum of the heart was observed. The woman and her family were informed in details with phenotypic malformation characteristic for carriers of trisomy 18. Conclusion: After consultation, parents decided to terminate this pregnancy, and it was done at 18th gestation week. Findings of pathologist confirmed all observed ultrasound congenital fetal abnormalities. Early prenatal diagnoses, continued pregnancy control, particularly ultrasound examination during the first trimester of pregnancy are essential for health offspring. Identification and early discovery of congenital fetal abnormalities and karyotyping enable complete information for the future parents about health of their child.

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Isolated femoral hypoplasia in uterus: Case report and differential diagnosis

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Objectives: Description of ultrasound and associated anomalies essential for prenatal differentiation between isolated form of femoral hypoplasia and other complex dysplasia associated.

Material and Methods: Presentation of a case with unilateral bowing and shortening femur diagnosed in prenatal period. Review of the associated Syndromes with this ultrasound picture.

Case report and differential diagnosis: We report a gestation of a 30 year-old woman, that at the 22nd week ultrasound was described a bowing and shortening left femur. Ultrasound did not reveal other associated lesions. Latter ultrasound evaluation was similar, with no other anomalies. Pregnancy ended at 38th week of gestation, normal delivery, a male weighting 3,130g, Apgar Index 9/10/10. The newborn was evaluated clinically, showing a shorter left inferior limb. Radiology revealed a shorter left femur with bowing, a concave side with cortical thickening and a convex side thinner. Systemic evaluation confirmed an isolated form of femoral hypoplasia.

This case integrates the Syndrome of congenital bowing of long bones. The main differential diagnoses include isolated form of femoral hypoplasia, femoral hypoplasia with proximal deficiency, familial history, severe immunodeficiency and also severe congenital Syndromes. Campomelia is the most common complex syndrome with bowing and shortening of bones, combined with facial dysplasia and thoracic wall alterations. Isolated femoral hypoplasia has often spontaneous resolution in the first year of life.

Comment: Facing a bowing and shortening femur, it is important to verify the location of the lesion and mainly the association with other malformations. Isolated femoral hypoplasia has benign evolution.

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Prenatal diagnosis of achondrogenesis type I with increased nuchal translucency at 15 weeks of gestation – a case report

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Introduction: Achondrogenesis is a lethal chondrodysplasia that is divided into two types – type I and type II. The incidence is about 1 in 40,000. The type I form presented with short limbs, rib fracture, deficient or absent vertebral corpus ossification, narrowed thorax, enlarged head and fetal hydrops. The type II form characterized by the same finding, but the mineralization deficit is less severe. The diagnosis is recognized by ultrasonographic findings of severe short limb, large head, and lack of vertebral ossification.

Case report: A 21-year-old woman, gravida 1, para 0, had received regular prenatal care at our hospital since 10 weeks’ gestation. Routine ultrasound examination at 15 weeks’ gestation showed increased nuchal translucency (5.7mm in length), short limbs, narrowed thorax, large cranium, and lack of vertebral corpus ossification. These findings were consistent with a diagnosis of achondrogenesis. Termination of pregnancy was offered and performed at 16 weeks’ gestation. Postmortem plain radiographs revealed large undermineralized cranium, short rib, absent ossification of vertebral body, and short long bones; and unossified ischia, pubic bones, sternum, and sacrum. Achondrogenesis type I was confirmed.

Discussion: Differential diagnosis of skeletal dysplasia prenataally is not easy. Ultrasound is the main method to detect. Nuchal edema in achondrogenesis has been described in the previous literature. Ultrasonographic diagnosis of achondrogenesis is based on the triad of severe short limbs, large head, and lack of vertebral ossification. Besides these classical signs, increased nuchal translucency may be a specific feature of achondrogenesis.

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Study of the acuity of echografic diagnosis in fetal skeletal dysplasia


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Abstract: The estimated prevalence of skeletal dysplasia in the perinatal period is 1/4000 to 1/5000 births. Prenatal ultrasound diagnosis is important as it may facilitate family counseling and pregnancy management.

Objective: This prospective and observational study sought to determine the acuity of echographic diagnosis in fetal skeletal dysplasia.

Materials and Methods: Fifty-five fetuses with diagnosis of skeletal dysplasia were managed from 1990 to 2008. Ultrasound evaluation was performed by physicians and was repeated during prenatal period. The sonographic findings was compared to the neonatal diagnosis, what was performed by the pediatric and the genetic group and fetal necropsy. The coefficients of diagnostic agreement (KAPPA) for the most common types of bone dysplasias and for the diagnosis of lethality of the fetal bone dysplasias were also obtained.

Results. Moderate agreement between the prenatal diagnosis and neonatal diagnosis was observed for the acondroplasy (Cohen's was Kappa the 0.66), thanatophoric dysplasia (Cohen's Kappa was 0.59), osteogenesis imperfecta (Cohen's Kappa was 0.42) and also for the lethality (Cohen's Kappa was 0.57).

Conclusions: Prenatal diagnosis accuracy varies with the type of skeletal dysplasia. Sonographic markers of lethal forms of skeletal dysplasia has only a moderate correlation to perinatal death. In this way obstetric management may not be based only on the antenatal findings.

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Thanatophoric dysplasia type II

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Introduction: The skeletal dysplasias are rare diseases that can be diagnosed prenatally. Prevalence of 2.4 per 10,000. Thanatrophic dysplasia is the most common, caused by a mutation in the fibroblast growth factor receptor 3 gene (FGFR3). This novo mutation appearing sporadically with an incomplete ossification of the osteocites. There are two subtypes: type 1: curved femur compared prominent hypertelorism, micromelia and saddle nose. Type 2: Short bones straight, cloverleaf skull, is inherited by autosomal dominant mutations.

Materials and Methods: Pregnant women diagnosed with type II dysplasia thanatoforic confirmed postmortem. Obstetric ultrasound: 16.5 weeks, the fetus presents skeletal dysplasia, micromelia sharp, narrow thorax, abdomen globular, cloverleaf skull and face prominently. Pathology reports shortened bones of the extremities, curvature of the fibula, radius and humerus, femur and skull straight in clover for thanatophoric dwarfism type II. Report molecular study of the direct FGFR3 gene from a sample of DNA from peripheral blood by PCR amplification and mutation in P. Lys650Glu.

Results: Thanatophoric dysplasia is characterized by rizomelia, narrow thorax, prominent face, saddle nose, short members and long bones. It is associated with hydrocephalus, atrial septal defect, imperforate anus and radiocubital synostosis. The type II occurs in people with no family history.

Conclusions: The association of skull and clover micromelia specific thanatophoric dysplasia. Mutation p. Lys650Glu is new, sporadic cases and follows an autosomal dominant pattern of inheritance, and recommends the implementation of molecular prenatal diagnosis for the study of this mutation in future generations.

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Fetal aquiria

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Introduction: defects in the formation of limbs are a heterogeneous entity that represent one of the most frequent malformations. A terminal transverse defect is the absence of the structure of the distal member with preservation of normal proximal structures, called the absence of hand: aquiria, with a prevalence from 0.04-0.15 per 10,000 births. The pathogenesis of these genetic alterations is not known. There are two theories: a vascular insufficiency due to injuries such as biopsy corial or teratogenic substances such as thalidomide.

Materials and methods: Pregnant 21-year-old, smoking, asthma. Screening: low risk. Negative serology. Analytica is normal. Ultrasonography of the second quarter is aquiria right.

Results: members of the buds appear during the fourth week as a small elevation of the ventrolateral wall. Each bud is formed by a layer of mesenchyme covered by mesoderm. Subsequently there is a migration of muscle precursor skipping along with a progressive invasion of endothelial and nerve cells. This development is regulated by specialized signals that direct cell behavior. By the sixth week, the mesenchyme condenses to form the plaques of the hands and digital rays, and they form a loose mesenchyme, which disappears by apoptosis shaping fingers.

Conclusions: cases of major congenital malformations are a diagnostic challenge and management due to the low frequency of genetic syndromes and complex lesions. The fetal aquiria occurs by an alteration in the development of the primordium in very early stages of embryonic development. Ultrasound is useful to know early malformations presented.

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Prenatal ultrasound diagnosis of apert syndrome

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Apert Syndrome is one of the FGFR-related Craniosynostosis Syndromes. It is characterized by midface hypoplasia and syndactyly of the hands and feet. It may be associated with varying degrees of mental retardation. prevalence is 1 in 65000 to 100,000 newborns.

The diagnosis of Apert syndrome is based on clinical findings. Molecular testing can be useful for differential diagnosis.

Prenatal diagnosis of this syndrome has been reported through ultrasound screening for fetal anomalies. However, as most of the cases are "de novo" mutations and some of the ultrasound findings should be carefully searched for, many cases remained undiagnosed until birth.

The aim of this report is to show that prenatal diagnosis of Apert syndrome can be achieved with a meticulous 2D ultrasound examination.

We report two cases of Apert syndrome that were referred to our Genetics Unit because of vague ultrasound findings: ventriculomegaly, short limbs and “abnormal skull”. A diagnosis of Apert syndrome was suspected based on 2-D prenatal ultrasound findings on the skull, hands and feet: prominent frontal bone suggesting craniosinostosis and syndactyly of toes and fingers (“mitten glove hands”). The diagnosis was confirmed by postnatal physical examination.

After prenatal sonographic detection of anomalies suggestive of Apert syndrome, parents should be counseled about prognosis. Prenatal MRI may be useful and molecular testing through amniocentesis can be offered to confirm the diagnosis. However this is not always feasible in countries with low economic resources, were ultrasound suspicion may be the only clue to prenatal diagnosis.

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A fourteen case series of fetuses with single umbilical artery: Antenatal evaluation

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Aim: Evaluation and follow-up of fetuses with single umbilical artery (SUA) regarding associated anomalies and prognosis. Method: Fourteen fetuses with SUA were evaluated and surveyed until outcome. Results: From 01.01.2005-31.12.2008, fourteen fetuses with SUA were detected at different pregnancy weeks (pw). From nine cases with isolated SUA six healthy babies were delivered at term and had a normal neonatal evolution, while three pregnancies are in evolution at 33, 34 and 35wp. In two fetuses SUA was associated with intrauterine growth restriction (IUGR) and with a pathological Doppler pattern. From the two fetuses with IUGR, one fetus with normal karyotype was born at 34wp by caesarean section (CS) and had a good evolution while the second was born by emergency CS after a spontaneously induced labor and died. Medical abortion was induced in three cases where SUA was associated with multiple anomalies or aneuploidy: 1 fetus with Trisomy 18, dextrocardia, bilateral choroid plexus cysts; the second with lip and palate cleft, diaphragmatic hernia and interventricular septum defect; the third with diaphragmatic hernia, and polydactyly. Conclusion: The scan of the umbilical cord must be a part of the 1st and 2nd trimester screening protocols. If a SUA was found a level three ultrasound scan must be performed to exclude associated anomalies. We recommend invasive karyotyping if SUA is associated with abnormal ultrasound/biochemical screening or IUGR. If in a fetus with SUA IUGR occurs, a Doppler evaluation of the fetal hemodynamic must be performed and the delivery planned in context.

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Antenatal classification of fetal hydronephrosis: an interobserver agreement evaluation

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Dilation of the renal collecting system can be observed and measured by anteroposterior renal pelvis diameter (APD). Measurements variations are important due to the elastic nature of the fetal renal system.

Objective: To measure the degree of which two ultrasonographers concur in their respective antenatal hydronephrosis classification, based on single evaluation.

Materials and methods: One ultrasonographer physician pair measured 50 APD in 25 fetuses (mean gestational age: 33.4 ± 4.3 weeks). Each observer performed three measurements and the mean was considered. Both were physicians at an university fetal medicine center. Hydronephrosis was classified in absent (APD<5mm), mild (APD 5 to 9.9mm), moderate (APD 10 to 14.9mm) and severe (APD≥15mm). Inter-rater agreement of prenatal hydronephrosis classification was calculated by Cohen's Kappa with linear weighting and using a 95% limits for all categories. The percentages of agreement to categories were determined.

Results: For absent, mild, moderate and severe categories, overall percentage of agreement and the linear weighting Kappa (95% confidence interval) to antenatal hydronephrosis classification was 64% and 0.67 (0.52 to 0.81) respectively. The percentage of agreement to mild category was 42.9% (9/21), to moderate was 60.0% (9/15), and to severe was 88.9% (8/9).

Conclusion: The inter-rater agreement to hydronephrosis classification between physicians was good, but the percentage of agreement to mild category was low. Therefore we suggest that antenatal mild hydronephrosis must be classified based on a sequence of evaluations, considering different occasions.

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Intraobserver error and interobserver variation in the sonographic measurement of renal pelvis anteroposterior diameter and hydronephrosis diagnosis, in suspect fetuses

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Hydronephrosis is the most common abnormality detected on prenatal ultrasonography (1.4%). Dilation of the renal collecting system can be observed and measured by anteroposterior renal pelvis diameter (APD).

Objective: to quantify the intraobserver variation, interobserver variability in the sonographic measurement of APD and agreement on hydronephrosis diagnosis.

Materials and methods: Three observer pairs measured 38 APD in 19 fetuses (mean gestational age: 33.5 ± 4.2 weeks). Each observer performed three measurements. All of them were ultrasonographers physicians. The mean and standard deviation of the absolute and percentage differences between measurements and observers were calculated. Hydronephrosis was present when anteroposterior diameter ≥5mm. Inter-rater agreement of prenatal hydronephrosis was calculated by Cohen's Kappa, and 95% limits for each observers pair.

Results: Absolute intraobserver variation in measurement of APD was 5.2% ± 3.5%. Interobserver variation was 11.1 ± 10.0%. Overall percentage of agreement and Cohen's Kappa (95% confidence interval) to antenatal hydronephrosis diagnosis between observer 1 and 2 were 84.2% and 0.53 (0.18 to 0.87), between observer 1 and 3 were 89.5% and 0.71 (0.544 to 0.98), between 2 and 3 were 74% and 0.31 (0.50 to 0.60), respectively.

Conclusion: The intraobserver and interobserver variation was low, but the agreement to hydronephrosis diagnosis between physicians was not good. Because of extremely elastic nature of the fetal renal system we suggest to take the mean of three measurements in more than one occasion for the antenatal hydronephrosis diagnosis by ultrasonography.

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The risk of chromosome abnormalities in presence of bilateral or unilateral fetal pyelectasis

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Methods: In this study authors investigate the chromosome abnormalities detected in cases with prior fetal pyelectasis. Authors performed chromosome analysis in 302 cases because of fetal pyelectasis. Results: In 203 cases, pyelectasis was associated with other ultrasound anomaly, and in 99 cases, the pyelectasis was non-associated. In the associated cases, they found chromosome abnormalities in 3%, and without other ultrasound anomalies, this rate was 1%. In unilateral cases, authors performed 101 analyzes, and in bilateral cases 201 examinations. In unilateral cases, they found abnormal karyotype in 1%, and in bilateral cases in 3%. The over-all risk was 2.3% (LR=0.63).

Conclusions: Ultrasound plays important role in prenatal diagnostics. Considering that the risk is not higher than 1% both in unilateral and non-associated cases, only bilateral and associated cases indicate chromosome analysis.

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Findings of ultrasound abdominal screening in neonates. Assesment in 30.893 liveborns

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Aims: To evaluate a program of abdominal ultrasound (AU) screening in liveborns (LBs).

Methods: Prospective descriptive analysis of the AU screening performed in all LBs within their first days of life by our neonatologist’s team during 12 years.

Results: A total of 30,623 LBs were examined since 1997 to 2008. In 945 LBs (3%) the AU provided significant findings, mainly in the urinary tract (29.7/1000 LBs). Unilateral renal ectasies (609 cases) were almost three times more frequent in the left kidney (452) than in the right one (157). The same tendency was seen regarding hydronephrosis (67 left side vs. 24 right side). There were 19 LBs with unilateral kidney agenesia, and 18 with multicystic unilateral kidney. Other findings were 37 hypo/anecoic masses on the upper kidney pole related to adrenal hemorrhages (AH), that were eight times more frequent in the right adrenal gland (33 vs. 4). Three cases of suspected AH turned out to be neuroblastoma. Liver calcifications or cysts in spleen and ovary were rare findings.

Conclusions: Systematic neonatal AU allows early diagnosis of anomalies, mainly renal, not always diagnosed prenatally. Renal ectasies and hydronephrosis were found mainly in the left side, while AH occurred much more in the opposite. The feasibility, high yielding and innocuous character of the ultrasound might deserve its inclusion along with hearing and metabolic in routine neonatal screening.

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Prenatal diagnosis of abnormal male genitalia

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Hypospadias is one of the most common congenital anomalies in the United Kingdom, occurring in approximately 1 in 300 live male births. The cause of this abnormality is still unclear. It has genetic predisposition and has a recurrence risk of 7-14%. Embryological studies have demonstrated that, depending on where the urethral development arrests, the meatal opening can be anywhere along the shaft of the penis or, in more severe forms, within the scrotum or in the perineum. It can be associated with undescended testis or inguinal hernia or renal tract abnormalities.

We report a case with ultrasound findings of abnormal male genitalia diagnosed in the second trimester of pregnancy and compared it with postnatal clinical features. The features observed were anomalous distal morphology of the penis, small lateral folds and a small penis. A small soft tissue mass was noted in the midline along the perineum and was referred to the fetal assessment unit. She had further scans at 22.28 and 32 weeks which confirmed the same findings. No other anomalies were detected.

The postnatal pictures of the newborns' genitalia corresponded perfectly to the prenatal sonograms. No associated anomalies was seen. The recognition of this may help to distinguish between severe hypospadias and other genital abnormalities (e. g. ambiguous genitalia). The prenatal study of the genitals of the fetus not only helps to determine the sex, but also to detect anomalies which contributes to a great extent with counseling.

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**Mckusick-Kaufman syndrome – a case report**

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Hydrometrocolpos (HMC) is an unusual congenital anomaly very rarely reported on prenatal sonography. It can be caused by failure of the distal third of the vagina to develop (vaginal atresia). HMC may be a serious life threatening condition due to its compression sequelae and possible associated congenital anomalies.

The combination of hydrometrocolpos and postaxial polydactyly (PAP) is the cardinal hallmark feature of McKusick-Kaufman Syndrome (MKS). In the Amish, there is an incidence of approximately 1:10,000. In the non-Amish population, prevalence and incidence have not been estimated.

We report a case of a female stillborn, product of non-consanguineous parents with a fetal hydrometrocolpos detected at 32 weeks’ gestation. The pregnancy was uneventful until then. Two initial prenatal sonograms at 12 and 20 weeks’ gestation were normal. The 32 weeks’ ultrasonography revealed a large pelvic cystic mass and ascites, however the sonographic findings were inconclusive. The woman was admitted for preterm labor on the day after and a female fetus with marked abdominal distension and postaxial polydactyly of the left hand was delivered. Postmortem examination demonstrated hydrometrocolpos due to vaginal atresia causing elevation of the diaphragm and thoracic compression, meconium peritonitis leading to dense abdominal adhesions. A “postaxial minimus” was identified.

MKS is a rare autosomal recessive condition whose diagnose is based on clinical findings. The manifestations of MKS can be detected by prenatal ultrasound examination. It is characterized by a triad of PAP, congenital heart disease (CHD), and hydrometrocolpos, however cardiac defects may not be present.

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Chorioangioma – a case report

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Introduction: Chorioangioma is defined as a benign tumor of the placenta, composed of blood vessels and stroma, originates from primitive chorionic mesenchyme.

Case: A 21 year old women, has made obstetrical ultrasound examination at my department at 7 – weeks of pregnancy, and because of abnormal findings on chorionic site was referred to OB/GYN clinic. After one week investigations and observation, the results were: Normal embryo-CRL=9.8mm (7.1 G.A.), yolk sac, and existing chorionic tumor (57x30mm) with multiple hypoechoic areas suggestive for partial molar pregnancy, and (HCG-7500 I.U.). Through first and second trimester was treated with gestational progesterone till 20 G. A., intensively ultrasound monitored almost every month. Sonograms revealed normal fetal biometry and morphology, while placenta became thicker with multiple cystic areas. Protecting preterm delivery, she was hospitalized two times, at 30 and 33 G. A. and successfully treated with tocolysis. But at 35 G. A. she delivered prematurely, healthy neonate (2200/48) at breech presentation (Bracht), and the placenta was removed manually because of massive placental haemorrhage. Discussion: Chorioangioma is a vascular malformation, with incidence -1:4 -10 000 births, and can complicate the pregnancy with IUGR, premature labor, polyhydramnion.

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28 years old S. G. from Cuprija. Second pregnancy. By anamnestic information there were no previous pregnancies in the near and distant relatives related with any abnormalitis or hromozomopathy or teratogenic pathology. First pregnancy end without any problems and she deliver healthy baby. During this pregnancy her obstertricion dane two ultra-sound examination and general laboratori. All Results were in the referentional values for GA. No screening on any hromosomopathy were done. On the Department of G&O she came with pain in the stomach, several diareas and vomiting. Obstetrition findings were without any pathological elements. By 2D US I egzam pacinet measures were: AM 18/6 BPD 47MM//ABD45MM//FHR130/MIN//FMR positive. Large amount off AF for the GA, and in the end of the rump tumor with mixed texture 102x92mm. Incidenca 1:40000 deliveries Dg Grav hdb18/19 Teratoma sacrococcygeale Polyhidroamnion Pacient sand to the Institute of G&O in Belgrade where pregnancy was terminate by intilation of the hypertonic solution of NaCl.

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Teratoma Sacrococcygeal (Case Report)

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Goal: 28 years old S. G. from Cuprija. Second pregnancy.
Methodology: By anamnestic information there were no previous pregnancies in the near and distant relatives related with any abnormalities or chromosomopathy or teratogenic pathology. First pregnancy end without any problems and she deliver healthy baby.
Results: During this pregnancy her obstetrician has done two ultra-sound and general laboratory examinations. All Results were in the referential values for GA. No screening on any chromosomopathy was done.
Discussion: She came at the Department of G&O with pain in the stomach, several diarrheas and vomiting.
Obstetrician: Findings were without any pathology elements. By 2D US I examine the fetus and measures were following: GW 18/6, BPD 47mm, ABD 45mm, FHR 130 bpm, FMR positive. Large amount of AF for the GA and in the end of the rump tumor with a mixed texture with size of 102×92mm. Frequency is 1:40000 deliveries.
Dg Grav hdb 18/19 Teratoma sacrococcygeal Polyhydramnion
Patient was sent to the Institute of G&O in Belgrade, where pregnancy was terminated by instillation of the hypertonic solution of NaCl.
Conclusion: This case shows necessity of screening for chromosomopathy in the first trimester (NT double test).

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Acardiac Twinning – a case report

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Acardiac twinning is an unique complication of monochorionic placentation occurring in 1% of monozygotic twins and 1 per 35 000 pregnancies. We present a case where an acardiac fetus was incidentally detected during an investigation of preterm labor with polyhidramnios in a 22 weeks’ gestation. The patient was sent to Barcelona, where she was submitted to intrauterine treatment with percutaneous sonographically guided laser coagulation. (to interrupt blood flow to the acardiac twin). She delivered at 27 weeks’ after prom by caesarian. The neonate is still in the neonatal unit care, with a good evolution.

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Cardiofemoral index as a predictor of perinatal outcome in gestation complicated by alloimunization after previous intrauterine transfusion

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Introduction: The CFI is noninvasive method to predict fetal anemia. It is obtained dividing the measurement biventricular outer dimension by the femur length. Its accuracy to diagnosis fetuses with severe intrauterine anemia is good and remains after intrauterine transfusion (IUT).

Objective: to assess the applicability of the last CFI measurement to predict perinatal death and severe anemia at birth.

Methods: A cohort of 286 isoimmunized pregnancies was followed from 2001 to 2009. IUT was indicated for 142 fetuses based on its hemoglobin levels obtained at cordocentesis. The last CFI measurement was performed during the last week of intrauterine life (before birth or death) and it was taken for analysis. Severe anemia at birth was diagnosed based on a cord blood hemoglobin level less than 9.5g/dL. Accuracy of abnormal CFI (value above 0.59) to predict those fetal complications was calculated.

Results: Mean gestational age at the last IUT was 31.0 ± 2.8 weeks. Fetuses had undergone from 1 to 6 previous IUT (median 2). Perinatal death occurred in 20.4% and severe anemia at birth was present in 22.1% of 131 cases that were born alive. The sensitivity, specificity and negative prediction value - for an abnormal CFI - to predict severe anemia at birth, were 86.2%, 41.2% and 91.3%, and to predict perinatal death were 82.8%, 38.1% and 89.6% respectively.

Conclusion: Cardiofemoral index is a good noninvasive marker of perinatal outcome after a previous IUT, in high risk fetuses.

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Comparison of four ultrasonographic algorithms in predicting fetal weight in seven birth weight groups

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The accuracy of birth weight estimation was assessed in 962 patients with singleton pregnancy using different sets of widely accepted formulas for fetal weight estimation. Fetal biometry was obtained by ultrasound within 7 days before birth and the weight range was assessed in six birth weight groups subdivided by 500g intervals. Twelve ultrasonographic mathematical formulas were compared to predict birth weight and classified into four groups in relation to the presence and combination of the main fetal biometric parameters (abdominal A; biparietal diameter and abdominal parameters BA; femur length and abdominal parameters FA; biparietal diameter, femur length and abdominal parameters BFA). The BFA algorithm shows the most stable Results in all the seven weight groups, with a mean percentage error ranged from 6% to 8% and a systematic error lower than 3% even if with a high 95% predictive interval. The A algorithm prove the lowest mean percentage error in infants weighing >4,000g (p<0.01) with a capability to predict accurately birth weight to or within 5% and 10% of the actual birth weight in 63% and 88% of cases, respectively. The Results suggest that mathematical models based on three biometric parameters (BFA algorithm) appear to be the most accurate in predicting birth weight throughout pregnancy. The models based on abdominal circumference alone proved a high accuracy in predicting fetal macrosomia. In the very low birth weight group all the algorithms evaluated revealed a poor precision that limit its clinical usefulness.

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How to minimize maternal morbidity associated with vacuum extraction?

Pertti Kirkinen

Vacuum-assisted delivery exposes women to short- and long-term complications such as hemorrhage, perineal pain, infection, anal incontinence, stress-incontinence, sexual dysfunction and negative emotional experiences. On the basis of recent clinical studies and statistics in Nordic countries, factors associated with these are presented here:

A) Antepartal training. Some evidence of a preventive effect of perineal massage exists.
B) Antepartal risk factor recognition. Risk factors do not reveal individual risk nor properly predict safe and high-risk procedures.
C) Intrapartal assessment. Macrosomy and posterior occipital presentation increase the complication rate. Translabial ultrasonography for verifying obstetric status and fetal head movement is a promising innovation.
D) Proper technique. Appropriate selection of rigid and flexible cups, restriction of the number of pulls, duration of the procedure and excessive traction decrease injuries. Traction force indicators should be utilized more in practice and during training. Perineal support, controlled delivery of the infant’s head and avoidance of routine episiotomy protect against perineal trauma.
E) Good diagnostic accuracy and operative procedures regarding anal sphincter damage. These involve 2-D and 3-D ultrasonography, good analgesia, monofilament suture material and separate closure of internal and external muscles.
F) Good postpartal care of sphincter complications with physical therapy and psychological support. The risks at subsequent delivery seem to be concentrated in that group with severe postoperative symptoms or secondary operation.

By improving diagnostic accuracy and operative procedures in cases of anal sphincter injury we can in practice best promote maternal health, because this complication cannot be completely avoided during vacuum-assisted delivery. Development of intrapartal methods for predicting a difficult or unsuccessful procedure would further improve the outcome.

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Impact of lunar position on nuchal translucency in the first trimester of pregnancy

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Objective: To analyze whether the moon influences the amount of fluid behind the fetus' neck and consequently alters the outcome of first trimester screening for chromosomal abnormalities by measurement of nuchal translucency.

Methods: The data of 1023 consecutive singleton fetuses measured between 11+0 and 13+6 gestational weeks at the four key lunar positions across 63 lunar cycles was retrospectively analyzed. To take into account for gestational variation in nuchal translucency, measurements were expressed as the difference from the normal median nuchal translucency at the measured crown rump length (Delta-NT).

Results: The mean Delta-NT was -0.0185mm (standard deviation 0.6867) at new moon, 0.0266mm (0.7697) at full moon and 0.0403mm (1.2151) and -0.0039 (0.6777) for first and last quarter respectively. No significant difference between the mean Delta-NT at these four key lunar positions was found (ANOVA, p=0.9). There was also no significant difference between the mean Delta-NT on days with spring tide (new moon/full moon) and neap tide (first quarter/last quarter) (0.0025mm vs. 0.0161mm, p=0.9). There were no significant differences in age, weight, parity and smoking status between the investigated groups of patients. There were also no significant differences in crown rump length, gestational age and biparietal diameter between the investigated fetuses.

Conclusion: Although effects of the moon on human physiology have been suggested, the moon does not influence the amount of fluid behind the fetus' neck. Adjustment for lunar position is not required in the first trimester screening for chromosomal abnormalities.

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Doppler in diagnosis of myomas in pregnancy

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Introduction: Myomas, benign tumors of flat muscular tissue and connective tissue of uterus, are found in 150 of 300 in pregnancies and are more common in women in their late reproductive period. Subserous and intramural myomas are the most common while submucosal are rarer.

Results and discussion: We have observed patients with myomas discovered during pregnancies and patients with earlier diagnosis. Study has been conducted in the period of the last four years.

By following Doppler flow rate we made pregnancies screening in the first trimester. We analyzed flows in the uterus and myomas - intramural, submucosal and subserous. We did not screen the group of patients with myomas with stalk because we doctrinally accepted myomectomy in possible torsion or secondary necrosis.

The Results showed decreasing of resistant index from 0.80-0.95 to 0.60-0.75. Resistant indexes of artery arcuate are decreased.

In the risk group of decreased resistant indexes myomas during pregnancies, other eight women were intensively followed. In the period of purperium, considering the maintenance of myoma resistant index and negative family anamnesis, in arrangement with the patients, myomectomy was performed in 5 cases i.e. 40%. In all women undergoing surgery histopathological diagnosis of early discovered sarcomas of uterus was stated.

Conclusion: Myomas as entity must be observed not only in relation to possible premature delivery or spontaneous miscarriage, but also independently as a whole because of timely prevention of possible alteration of malignant process.

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The growth behavior of myomas during pregnancy

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Introduction: Fibroid of the uterus as the most common benign tumor in women is gaining importance in the obstetric management due to the increasing average age of pregnant women.

Method: From 2001 to 2007 we retrospectively analyzed 9715 deliveries at the Charité University hospital, Campus Mitte of which 96 patients (0.98%) presented with uterine fibroids. In addition we reviewed the notes of 171 outpatients where uterine fibroids were diagnosed during a routine prenatal diagnosis examination.

Results: Precise measurements of the myoma were recorded in 349 of 375 cases (93.0%). 260 (74.5%) myoma were smaller than 50mm, whereas 89 (25.5%) measured 50mm or more. After loss to follow up exclusion we were able to analyze 99 measurements of 71 myomas. 40.4% altered in size by less than 10%. They can therefore be looked at as virtually unchanged. There was no statistical difference in growth during pregnancy when correlated to each trimester. Comparison of each trimester regarding growth of fibroid and its initial size (up to 50mm and larger than 50mm) did not lead to a significant difference.

Conclusion: Our Results indicate that a prediction of fibroid growth in pregnancy is not feasible. We can neither define a gestational age at which fibroids would show a tendency to grow in size nor if they will be rather increase or decrease in size.

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**Left ventricular and myocardial function in healthy and pre-eclamptic pregnancies: A study design**

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Objective: The aim of our study is to evaluate echo assessment of Left Ventricular (LV) and myocardial function in healthy pregnancies and in those complicated by severe pre-eclampsia.

Materials and methods: This is a retrospective observational study. Women enrolled are stratified into 3 groups: healthy women (group 1), normal pregnancy (group 2) and women with severe pre-eclampsia (group 3). Women (group 2, group 3) are enrolled at the time of morphological ultrasound examination. Women of group 1 are healthy-patients undergone to a cardiac exam. Exclusion criteria are: women with known hypertension or heart and renal diseases and twin pregnancies.

Timing of cardiac ultrasound examination is (group 2 and 3):
- I: at 20-21+6 week.
- II: at 29-30+6 week.
- III: until 1 month post-partum.

Group 1: during cardiac evaluation.

Echo assessment to consider:

**LV Morphology:**
- diastolic and systolic dimensions
- wall thickness
- mass

**LV Systolic Function:**
- ejection fraction
- stroke volume and cardiac output
- twist and untwist
- longitudinal, circumferential and radial strain
- myocardial velocities of 6 ventricular walls
- filling
- pulmonary vein
- E wave propagation velocity

**LV Diastolic Function**
- Systemic Vascular Resistance
- Right Atrial Pressure
- Pulmonary Systolic Pressure

Conclusions: We expect to find physiological ultrasonographic features of healthy pregnancy. In a second time, we will expect to find pathological echo assessment in pregnancies complicated by preeclampsia to detect some ultrasonographic risk factors for this severe complication to optimize its therapeutic management.

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The “hypotenuse test”: A new ultrasonographic method in predicting fetal overgrowth in diabetic and non-diabetic pregnant women

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The accuracy of 17 formulas and the role of single fetal biometric parameters used for the estimation of fetal weight in diabetic and non-diabetic pregnant women delivered large for gestational age newborns. The study group consisted of 333 fetuses examined by 2D ultrasound within seven days before birth. Seventeen mathematical formulas were tested using the mean absolute percentage error, standard deviation, accuracy in prediction within ±5%, ±10%, ±15% of error and introducing a new variable labeled “hypotenuse test” which can sum up precision and accuracy of the formulas employed. The formulas were assessed and clustered in four algorithms (X, Y, Z, W) on the basis of fetal biometric parameters that they incorporated. The lowest mean percentage error, standard deviation and hypotenuse test were seen with Warsof’s equation (p<.01) with overall prediction ±5%, ±10%, ±15% of the actual birth weight of the 68%, 94% and 98%, respectively. Among the four different algorithms, the formulas based only on the abdominal measurements (X algorithm) showed the lowest mean absolute percentage error in large for gestational age fetuses of diabetic women (p<.05). The new test proposed in the study (“hypotenuse test”) appears to be particularly helpful ever since it can sum up precision and accuracy of tested formulas. The accuracy of sonographic fetal weight estimation in large for gestational age fetuses may be attributable to the biometric parameters used to derive weight equation. Our findings show that the best formulas for predicting birth weight are those considering only abdominal measurements, particularly in diabetic pregnancies.

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**Labor and perinatal complications in macrosomic fetuses**

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This retrospective study evaluate the influence of birth weight at delivery in the obstetric management and maternal and neonatal morbidity. The study group consisted of 11821 women who delivered 1237 macrosomic infants (437 of diabetic and 800 of non-diabetic pregnancies) and 10584 non macrosomic infants (reference group). The macrosomic fetuses were subsequently grouped in relation to birth weight: 4,000-4,250g, 4,251-4,500g and >4,500g. Route of delivery, indications for caesarean section, maternal complications and neonatal outcome were determined in order to evaluate the role of macrosomia and diabetes. The incidence of caesarean section because of alteration in the 2nd stage of labor, frequently associated with a relatively high incidence of fetal trauma and complications, was 33.1% in diabetic macrosomic fetuses, comparing to the 25.9% in the reference population. Besides, the overall risk of shoulder dystocia is higher in macrosomic fetuses (p<0.01) and rises sharply in relation to birth weight (1.2% in fetuses weighing <4,000g; 7.9% from 4,000 to 4,250g; 11.8% from 4,250 to 4,500g; 16.0% >4,500g) particularly in diabetic pregnancies. Neonatal pulmonary complications appear to be higher in macrosomic groups, particularly when complicated by maternal diabetes (p<0.01), with a rise in relation to birth weight. Our Results suggest that a particular attention should be paid in macrosomic infants and that the incorporation of different steps of weight in the definition of fetal macrosomia may be more useful than a simple birth weight cut off value in the clinical management.

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**Ultrasonographic evaluation in first trimester pregnancy at patients with obstetrical antiphospholipid antibody syndrome**

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Objective: Obstetrical antiphospholipid antibody syndrome (OAPS) represents the clinical syndrome focused on infertility and pregnancy morbidity, together with the biological syndrome (aCL, LAC, anti ß2-GPI antibodies). Our research is targeting to evaluate the ultrasonographic aspects occurring at patients with OAPS in first trimester of pregnancy.

Methods: Our study has been developed on a lot of 462 pregnant women diagnosed with OAPS, between 10/2004 and 1/2009. All patients received 2D/3D transabdominal or transvaginal examination. OAPS diagnosis has been accomplished using both Sapporo and Sydney criteria. Seronegative OAPS has been diagnosed in 12 cases. All of the patients were receiving specific therapy.

Results: Ultrasonographic examination in the first trimester at women with OAPS has been carrying out the following aspects: intrauterine pregnancy diagnosis, pregnancy viability, gestational age evaluation, Doppler hemodynamic profile in utero-placental blood flow, nuchal translucency measurement, cervical length measurement, gestational trophoblastic disease diagnosis – 4 cases (0.86%), multifetal gestation – 17 cases (3.67%). Early pregnancy failure has been diagnosed in 49 cases (10.6%). There have been diagnosed 15 twin pregnancies and 2 triplet pregnancies. Vanishing twin syndrome has been diagnosed in two cases.

Conclusions: Ultrasonographic evaluation in the first trimester is representing a first priority for OAPS pregnancies. The prevalence of modifications in Doppler hemodynamic profile from OAPS is equivalent with normal pregnancy. Standard therapy is significantly improving the Doppler hemodynamic profile in OAPS depending on the anticoagulant therapy. Ultrasonographic evaluation in the first trimester is significantly diminishing pregnancy morbidity in OAPS.

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Prenatal and postnatal neurological evaluation of infant from pregnancy complicated with IUGR and fetal hypoxia

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A 34-year-old pregnant woman, grav 3, para 1, peur 0, non-smoker, with a history of renal infection and diagnosed cervical insufficiency was admitted to the hospital at 27 weeks of gestation (wg) because of asymmetric fetal intrauterine growth restriction (IUGR). At hospitalization the Doppler ultrasound examination showed fetal flow redistribution with increased brain perfusion, and absent end-diastolic flow of the umbilical artery indicating fetal hypoxia. We have shown that severe brain damage can develop despite the fetal blood flow redistribution and increased brain perfusion. Therefore, we applied our new prenatal neurological screening test which is based on specific fetal movement patterns and signs observed by four-dimensional ultrasound. According to total score the following subgroups are: abnormal (0-5), moderately deviant (6-13) and normal (14-19). Fetal score was from 13 to 14 placing the fetus in moderately deviant and/or normal subgroup. At 30 wg preeclampsia occurred and pregnancy was ended by an emergency caesarian section (infant weight: 940g, APGAR 10, 10). Postnatal ultrasound brain examination showed bilateral intraventricular hemorrhage gr II. Amiel Tisson’s neonatal assessment test was repeated every 2 weeks until the end of hospitalization showing normal neurological status. General movements (GMs) by Hadders-Algra were assessed at preterm, writhing, and fidgety age and each time classified as normal-suboptimal GMs. With 15 months of life child is demonstrating normal neurodevelopment. Despite unfavorable intrauterine conditions, diagnosed IUGR and fetal hypoxia, this premature infant showed normal neurological development which was verified not only by postnatal tests but also with new prenatal neurological screening test.

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Fetal hyperechogenic bowel and early necrotizing enterocolitis; in three intrauterine growth restricted, extremely low birth weigh infants

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Hyperechogenic Bowel (HEB) can be found in 0.1-1.8% of pregnancies as a normal variant in fetuses, during the second or third trimester. Some researches reveal that in the second trimester HEB is the marker of subsequent suboptimal fetal growth. Intrauterine growth restricted (IUGR) has been expected to complicate 4% to 18% of pregnancies with HEB.

In this study we presented 3 cases who had severe IUGR, fetal absence of reversal of end diastolic flow in umbilical artery and severe HEB, at the end of second trimester. One of them gave birth at 28 weeks because of severe preeclampsia and two of them at 29, 30 gestational weeks because of fetal distress. Birth weighs were 930, 760 and 850 grams, respectively. All the three infants had abdominal distention and discoloration at abdominal skin without feeding in the first hours. Radiographic grade II necrotizing enterocolitis (NEC) was diagnosed in the first 48 hours and antibiotics and total parenteral nutrition were given. Eventually, enteral feeding had been able to start at the fourth week in all the three babies. None of them had perforation or short bowel syndrome afterwards.

We think that HEB is an important finding to make a decision about timing of delivery and predicting NEC at early neonatal period.

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Clinical efficacy of cervical length measurement for the prediction of high risk VBAC candidates
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Objectives: Vaginal birth after caesarean section (VBAC) is association with a small but significant risk of uterine rupture with poor outcomes for both mother and infant. Any attempt to induced labor increases the risk of uterine rupture in VBAC. Our objective is to determine whether cervical length predicts risk of postterm induction of VBAC.

Methods: This prospective study was conducted in 114 patients of VBAC out patient clinic. Cervical length was measured by a 7.5-MHz transvaginal transducer between 36+0 and 37+6 weeks of gestation. The primary outcome was the rate of deliveries after 41 weeks. We constructed a receiver operator characteristic (ROC) curve to determine the optimal cut-off point of the cervical length, to predict postterm delivery.

Results: 32 (28%) patients was delivered after 41 weeks. The ROC curve showed that the optimal cut-off point of cervical length was 2.4cm. The predictive values of cervical volume on delivery after 41 weeks weeks were: 87.5% of sensitivity; 23.2% of specificity; 82.6% of negative predictive value; 30.8% of positive predictive value, respectively.

Conclusion: This paper is one of a series that will address patient factors, hospital factors, and clinical policies associated with VBAC outcome. The cervical length assessment is good tool in predicting postterm delivery. Long cervical length could be considered clinical risk factor of VBAC. After further study, that will be used informed consent, risk assessment and selection of candidates.

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Deep vein thrombosis is a common cause of morbidity and mortality in certain high-risk groups such as gynecological and oncologic surgery patients and pregnant women. Normally the external and common iliac veins can be visualized by transabdominal ultrasound but during pregnancy gravid uterus often limits the examination of these vessels. This report describes a case of thrombosis starting from the proximal half of the tibial vein and extending to the iliac vessels. A 25 year old G3/P0 woman with heterozygous Factor V Leiden Mutation was referred at 26 weeks of gestation to our hospital. Despite LMWH prophylaxis a left-sided thrombosis of the lower extremity and thigh occurred. Transcutaneous Color Doppler led to the diagnosis of thrombosis of the left upper thigh. However, the proximal portion of the thrombus could not be visualized because of the gravid uterus. Transvaginal ultrasound and Doppler were performed (5-9 MHz vaginal probe, Voluson 730 Expert ultrasound system, Kretz, Austria). B-Mode examination of the iliac vessels on the left side indicated complete occlusion of the common iliac vein. The occlusion was verified using Color Doppler and there was no flow visible in the left common iliac vein. Doppler is the standard diagnostic procedure for vein thrombosis. However, transabdominal ultrasound is limited in the detection of pelvic vein thrombosis during pregnancy due to poor acoustic window. Therefore a transvaginal approach in pregnant patients should be considered. This report demonstrates the feasibility of transvaginal sonography for visualizing venous thrombosis in the pelvic vessels in pregnancy.
Correlation between transperineal sonography and open magnetic resonance imaging to determine head station in pregnant women at term


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Objectives: During labor the transperineal sonography is becoming an established method to evaluate of labor progress and success rate for a ventouse. Otherwise, the ischial spines, the maternal landmark in vaginal examination, cannot be visualized by ultrasound, but with magnetic resonance imaging (MRI). The aim of this study was to examine the correlation between the station of the presenting part at term measured by transperineal ultrasound and open MRI. Methods: 12 pregnant women at term (>37 weeks), who were not in labor, underwent an open MRI. The ischial spines were located in a parasagittal plane and the corresponding interspinal level was identified in a midsagittal plane. The distance between the presenting part above the interspinal level was scaled. Immediately after MRI, without changing the supine position, a translabial ultrasound using a Voluson 730 expert machine was performed. The angle of progression formed between a line placed through the midline of the symphysis pubis, and a second line drawn from the inferior apex of the symphysis tangentially to the fetal skull was measured by ultrasound and MRI. Results: Angle of progression measured by ultrasound (mean 77.75° STD 8.2) and MRI (mean 79.48° STD 6.5) correlated significantly (p<0.001). A linear regression was found between the angle of progression in transperineal sonography and the distance from the presenting part to the ischial spine line in MRI (p<0.001; r²=0.84). An angle of 100-110° would be corresponded with engagement (station 0). Conclusion: Transperineal ultrasound brings objectivity to the assessment of fetal station. The angle of progression measured by transperineal sonography and MRI correlated well. The geometric model from Barbera et al., in which an angle of 99° corresponded with engagement, was confirmed in vivo.

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Correlations of fetal-maternal outcomes and first trimester 3-D placental volume, 3-D power doppler calculations

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Objective: The purpose of this study was to investigate correlations between first trimester placental volume, placental vascularization indexes and the outcome of those pregnancies. The possible prediction of macrosomia and intrauterine growth restriction in the first trimester will be searched.

Methods: We prospectively examined 145 pregnant patients at 11-14 weeks of gestation using transvaginal 3D gray-scale and power Doppler ultrasound. The acquired volumes were analyzed using the VOCAL imaging program, for assessing placental volume, vascularization index (VI), flow index (FI) and vascularization flow index (VFI). The Results were correlated with the pregnancy outcome.

Results: Correlation between placental volume and intrauterine growth restriction group of infants classified according to their anthropometric measurements was significant. As the placental volume decreases, percentage of intrauterine growth restriction increases. In the aspect of placental vascularisation indexes, VI showed a positive linear correlation with newborn weight.

Conclusion: The 3 dimensional placental volume and blood flow calculations could be important in the prediction and easy, rapid diagnostic evaluation of fetal growth restriction presenting with placental volume and vascular tree alterations even at the first trimester.

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Result of gestation with pathological doppler of middle cerebral artery and umbilical artery of fetus

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Aim: the work it is the investigation of anormal waveforms of flow of Doppler of middle cerebral artery of fetus and umbilical arteries as indicator for fetoplacental circulation aiming at the use as diagnostics of method of intrauterine growth restriction (IUGR) and embryonic hypoxemia.

Material-method: The work concerns pregnant that were examined into the exterior rooms of Obstetrical clinic of Hospital of Pyrgos. After the 32nd week of gestation pregnant women were submitted to Doppler of middle cerebral artery of fetus and umbilical arteries, from them 16 pregnant women presented anormal waveforms.

Result: In 16 pregnant women was presented increase of blood flow in the brain of fetus can be realized with the examination Doppler of middle cerebral artery of fetus, the pulsatility index (PI) of middle cerebral is smaller than the physiologic prices for the age of gestation and increased diastolic flow then the partial pressure of oxygen in the umbilical artery is decreased (at 2-4 divergences). Absence of telodiastolic flow into the umbilical artery. The abdominal circumference of fetus becomes smaller than the 5th centesimal place, the amniotic fluid begins to be decreased. There presented palmic waves in the wave of flow of umbilical vein, Increase Pi, Reversed a – wave in Ductus venosus. Usually in 2-3 days follow pathological cardiotocography test (NST) From this 15 gave birth IUGR nursling. Existed a intra-uterine death.

Conclusion: The diagnostics method of anormal waveforms of flow of Doppler of MCA of fetus and of the UA, DV, is high sensitivity compared to NST.

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Axonal loss in the optic nerve of five-year-old children born small-for-gestational age at term

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Objective: Small-for-gestational-age fetuses with normal umbilical artery (UA) Doppler are currently defined as normal small fetuses, but recent evidence suggests that a substantial proportion of these fetuses have true growth restriction. Our aim was to evaluate the retinal nerve fiber layer (RNFL) thickness in term SGA fetuses with normal UA, since the optic nerve is a part of the central nervous system.

Methods: A complete ophthalmic examination that included visual acuity and optical coherence tomography (OCT) at age 5 years was performed in a cohort of SGA term fetuses with normal umbilical artery Doppler and compared with gestational age and sex-matched appropriate-for-gestational age (AGA) infants. Mann-Whitney U test was used for statistical analysis.

Results: A total of 24 children (10 SGA and 14 AGA) were included. Mean birth weight and gestational age was 2,146g and 38.3 weeks respectively among SGA fetuses. No differences were found for visual acuity, social or demographic variables between both groups. SGA fetuses showed statistically significantly lower RNFL thickness both for temporal (56 µ vs. 71.38 µ; p<0.05) and inferior (117 µ vs. 131.69; p<0.05) quadrants. A non statistically significant trend to decreased mean RNFL thickness (97.56 µ vs. 103.73 µ; p=0.07) was also observed in SGA group.

Conclusion: We detected a decreased RNFL thickness in term SGA fetuses with no signs of placental insufficiency. Axonal loss in the optic nerve of these children shows a neurological damage, which could indicate a sign of subclinical injury of the central nervous system.

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Evaluation the compared doppler ultrasonography and serial fondal height measurement in detection of IUGR

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Abstract
Introduction & Objective: There are different method for detection of fetal growth restriction. The important of this are serial fondal height (SFH), and ultrasonic measurement. Because of sensivity and specificity in different studies are variable. We evaluate the comparison between sensivity and specificity of SFH (a safe and simple method) with Doppler ultrasonography in F. G. R.

Materials & Methods: This study was cross-sectional and we selected 550 pregnant women with growth retardation in physical exam more than 4cm in SFH. so they referred to Doppler ultrasonography. we matched demographic character, obstetrics history, B Mode sonography finding (AFI/ placental grading) and evaluated in last records of neonatal weight / and other records for IUGR. We analysis sensivity and specificity of SFH and Doppler ultrasonography in detection of IUGR.

Results: The average age was 22.5 4.9(16-45), average of Parity was 1.3 0.7(1-11). Prevalence of IUGR in population study was 9.4% and sensivity and specificity of SFH in detection of IUGR 44/7%,93.8% respectively with positive predictive value 44.8% and negative predictive value 94.6%, Doppler ultrasonography sensivity and specificity was 90.9% and 100% respectively.

Conclusion: Our study propose that SFH in detection of IUGR is valid measurement and draw growth curve is necessary.

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The nucleated red blood cell counts in the cord blood with intrauterine growth restriction in term pregnancy

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Objective: To determine the relationship between nucleated red blood cell in the umbilical cord (nRBC) and Doppler wave form velocity with intrauterine growth restriction (IUGR) in term pregnancy

Methods: Total 93 cases were enrolled and were categorized according to S/D ratio of umbilical artery. Patients were classified as normal pregnancy (n=22), normal S/D ratio group (n=60), and abnormal S/D ratio group (n=11). All cases were delivered at 37+0-41+6 weeks of gestational age from January 2001 to December 2008 at Ajou University Medical Center. The criteria for S/D ratio of umbilical artery was 3.0 and the neonatal weight <10 percentile compared to gestational age was used for definition of IUGR. Gas analysis and blood tests, including nRBC count in umbilical artery, were done during delivery.

Results: The abnormal S/D ratio group showed significantly higher numbers of nRBC compared to the other groups (2.25 vs. 4.67 vs. 8.91/WBC100, p<0.05). Also there was a significant decrease of neonatal weight in the abnormal S/D ratio group compared to the other groups (2,130gm vs. 2,420gm vs. 3,211gm, p<0.005).

Conclusions: The number of nRBC of the umbilical artery showed an increase in the group of abnormal S/D ratio and associated with decreased neonatal weight.

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Effects of abdominal warming using a heat- and steam-generating sheet on uterine blood flow

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In Japan, a loose-knitted warm abdominal band, haraobi, is generally used by pregnant women since it has been believed to exhibit favorable effects on the uterus and fetus. Abdominal warming has also been used widely as a non-pharmacological treatment to relieve dysmenorrhea. In this study, we investigated the effects of the abdominal application of a heat- and steam-generating (HSG) sheet of 54cm², which warms the skin where it is attached to at around 38.5 Celsius degree for 5 to 8 hours, on the relief of dysmenorrhea-related pain and uterine blood flow of women to obtain basic data on the physiological responses of women to abdominal warming. We tested the effects of pain relief of 1-hour abdominal HSG sheet application in 27 women (mean: 21.1 years old) on the second day of menstruation. Self-reports of pain relief revealed that 52% of the subjects reported the relief of dysmenorrheic pain. We also examined the effects on uterine blood flow of abdominal HSG sheet application for 5 to 8 hours in eight women (mean: 22 years old) on the 2nd day of menstruation. We measured systolic (Vmax) and diastolic (Vmin) velocities of uterine blood flow using Doppler flowmetry employing ultrasonography, and evaluated changes in the resistance index (RI; 1-Vmin/Vmax). The mean RI decreased in five of the subjects whose menstrual pains were relieved by HSG sheet applications. These results suggest that the warming of the abdomen by HSG sheet may increase uterine blood flow and exhibit favorable effects.

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Utility of uterine artery doppler flow mediation at 20 gestation weeks and the follow-up at 26 weeks and in the third quarter

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Objectives: To value the utility of uterine artery Doppler (UAD) flow at 20th week ultrasound and the follow-up in cases with abnormal flows and the study about perinatal outcomes.

Materials, methods and results: Prospective cohort study with statistical computerized analysis with SPSS-PC+ was designed to study UAD flow in the 20th week ultrasound in 1169 pregnant during year 2008 in our hospital. There were normal flows in 92% of total. We repeated UAD at the 26th week and we obtained abnormal flows in 1.6%; and flows were pathological too in the third quarter in 2.1%. (abnormal UAD flow was defined as index of pulsatility >p95)

We studied the distribution of altered flows in different moments of gestation according to groups of low, half and high risk; statistically significant Results being observed to 26 weeks and the 3r trimester (p=0.001) but not in 20 weeks (p=0.007). We studied the relation between abnormal flows and different obstetric variables: weeks of gestation, percentile of estimated weight by ultrasound in the third quarter, the weight of the newborn and Apgar in the first minute were statistically significant all of them (p=0.001)

Conclusions: The follow-up in patients with altered Doppler is useful at the 20th weeks, 26th weeks and the third quarter. The measurement of UAD is recommended all pregnant women at 20 weeks because abnormal flows in patients without factors risk is related with uterus-placental immaturity. A pathological UAD in the second quarter may be a scoreboard of worse perinatal outcomes.

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The importance of unilateral pathological doppler of uterine artery in the gestation

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Aim: Its the investigation as diagnostics method of IUGR and preeclampsia the use of unilateral abnormal waveforms of flow of Doppler of uterine arteries.

Material-method: The study of the maternal and embryonic Result from pregnant that was examined in Hospital of Pyrgos the last five years. During the ultrasound examination was studied the flow of Doppler in the division of uterine artery with the internal iliac artery in 20th until 24th week of gestation and was realized the presence of diastolic notches or the increase of pulsatility index (PI) (to be bigger the 95th centesimal place) in the wave flow of Doppler of the one of uterine artery in 40 pregnant. The control team was 40 pregnant, that presented normal waveforms of flow of Doppler of uterine arteries in the same age of gestation. Statistical analysis became with method SPSS.

Result: In the team pregnant with unilateral abnormal waveforms of flow of Doppler of uterine arteries, were diagnosed three incidents with intra-uterine delay of growth, three incidents preeclampsia and no abruption of placenta or intra-uterine death. In the control team of pregnant with normal waveforms of flow of Doppler of uterine arteries were diagnosed two incidents with intra-uterine delay of growth, two incidents of preeclampsia and no case of abruption of placenta and intra-uterine death.

Conclusion: The presence of unilateral abnormal waveforms of flow of Doppler of uterine arteries is not from alone her diagnostics method for the intrauterine growth restriction and for the growth of preeclampsia.

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Observation of umbilical arterial curve in nuchal cord encirclements with normal late third trimester pregnancies and pre-eclampsia

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Objective  To evaluate overall the variety curves of umbilical arterial flow dynamics in color Doppler ultrasound measurements by checking fetal end of umbilical artery, drifting segment, placental end of the umbilical artery. To study the correlation between pregnant outcome and umbilical arterial flow dynamics among nuchal cord encirclements with normal late third trimester pregnancies and pre-eclampsia.

Material and Methods  57 patients with pre-eclampsia are defined as study group, 21 cases are nuchal cord encirclements among them. 177 cases normal pregnancies are matched control group, 50 (nuchal cord encirclements). The umbilical artery sample parts include fetal end of umbilical artery, drifting segment, and placental end of the umbilical artery.

Result  The normal blood dynamics variety regulation of the umbilical artery blood curve is that from high toward low constantly. The average value of umbilicus blood during the fetus end and placenta end of umbilical artery approach to the value of the drifting segment. The value in pre-eclampsia is higher than that of the normal pregnancies in each point, the curve is similar. The occurrence rate of the complications in pre-eclampsia with nuchal cord is higher than the matched control group.

Conclusion  In the normal group, the umbilicus blood S/D, PI values are descending curve characteristics from the fetal end to the placental end of the umbilical artery. The position of the normal umbilicus blood examination should be the drifting segment. The three points should be measured in nuchal cord encirclements with normal late third trimester pregnancies and pre-eclampsia.

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Assessment of the abnormal uterine artery Doppler flow velocimetry, the risk of pre-eclampsia and indices of arterial structure and function

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Background and Aim: Pre-eclampsia increases the risk of future cardiovascular disease. We investigated the association between abnormal uterine artery Doppler flow velocimetry, risk of pre-eclampsia and several indices of arterial structure and function.

Methods: The carotid intima-media thickness (cIMT; a surrogate marker for atherosclerosis and predictor of future cardiovascular events) of 34 pregnant women with normal uteroplacental flow was compared with 30 women with abnormal uterine artery Doppler analysis (mean pulsatility index [PI] ≥1.6) during the transvaginal assessment of the uterine arteries at the routine anomaly scan (20–23 weeks of gestation). Pulse wave velocity (PWV) and brachial flow mediated dilatation (FMD) were also measured.

Results: Women with abnormal uterine artery PI had a greater mean internal (but not common) cIMT (0.58±0.06 vs. 0.53±0.08, respectively; p =0.005) and risk of developing pre-eclampsia (6 of 30 vs. 0 of 34, or 20% vs. 0%, respectively; p =0.0079) compared with those with normal uteroplacental flow. PWV and FMD did not differ significantly between the groups.

Conclusions: Women with abnormal uterine artery Doppler Results may be at increased risk not only of developing subsequent pre-eclampsia but also future cardiovascular disease. This increased risk may be present prior to and/or independently from the development of pre-eclampsia. Abnormal uterine artery Doppler Results at 20-23 weeks of gestation may be a prognostic marker for future cardiovascular disease and events.

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A pilot screening for preeclampsia by oxidative stress markers and uteroplacental blood flow

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Aim: Recent evidence suggests that the oxidative stress is an important factor in the pathophysiology of pre-eclampsia. The purpose of this study was to evaluate the possible relationship between increased resistance at the Doppler assessment of the uterine arteries between 20-23 gestational weeks and biochemical markers of oxidative stress, with the development of pre-eclampsia and/or growth restricted infants.

Material-Method: This was a prospective study of 34 pregnant women with normal uteroplacental flow and 30 women with abnormal uterine arteries Doppler analysis (mean PI ≥1.60) during the transvaginal assessment of the uterine arteries at the routine anomaly scan. Blood samples were obtained in order to assess the plasma oxidative stress, namely malondialdehyde (MDA) and uric acid levels.

Results: The MDA was significantly higher in the group of women with abnormal uterine arteries Dopplers (1.65±0.69 vs. 1.27±0.42µM, respectively, p =0.005). This group is at increased risk for the development of pre-eclampsia. The uric acid levels did not differ significantly between the two groups of women (3.50±0.69 vs. 1.27±0.59mg/dl, respectively, p =0.814). There was no significant difference regarding the sensitivity or the specificity of the uterine arteries Doppler examination in detecting pre-eclampsia in comparison to the combination of oxidative stress and Doppler’s.

Conclusion: Our study provides additional evidence regarding the role of oxidative stress in the pathophysiology of pre-eclampsia. Whether antioxidant supplementation in the group of women with abnormal uterine Doppler’s is effective in reducing the incidence of the disease remains to be established.

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Longitudinal examination of cervical volume and vascularization changes during antepartum and postpartum period using three-dimensional ultrasound and power doppler ultrasound

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Objective: To assess longitudinal changes of cervical volume and vascularization during antepartum and postpartum period using 3D ultrasound and power Doppler and secondly, to determine whether the measures used change with gestational complications.

Methods: A longitudinal study of cervical dimensions obtained by transvaginal 3D US and power Doppler using virtual organ analysis (VOCAL) program were performed at 11-14, 22-24, 32-34 weeks' gestation and postpartum 6th week in 111 pregnant women. Results: Cervical volume increased 4.4cm³ between 1st and 3rd trimester and decreased 19.2cm³ after 3rd trimester till postpartum 6th week. Cervical vascularization index VI (%) increased %2 between 1st and 2nd trimester, didn’t change during 2nd trimester and decreased %5.4 between 3. trimester and postpartum 6th week. There was no change in the flow index (FI) between 1. and 3. trimester; decreased 4.7 after 3rd trimester till postpartum 6th week. VFI increased 0.7 between 1st trimester and 2nd trimester, didn’t change during the 2nd trimester, and decreased 0.21 after 3rd trimester till postpartum 6th week.

Conclusion: Reference values for cervical volume and blood flow indices as assessed by 3D power Doppler ultrasonography are presented for every trimester of pregnancy and postpartum period. Measuring cervical volume and vascularization may not get any additional benefit in prediction of preterm labor and gestational diabetes. Using the 3D USG and power Doppler in cervical volume and vascularization measurement may be useful in the prediction of preeclampsia and this may lay the basis for further studies.

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Ductus venosus doppler velocimetry evaluation in first-trimester ultrasound screening

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Objectives: First-trimester ultrasound screening of nuchal translucency thickness (NT) and ductus venosus (DV) is a tool for assessment of fetal risk of aneuploidy and other adverse outcomes. The goal of our study was to prove, that DV examination leads to better results in discovering of fetal structural abnormalities, genetic disorders, and that abnormal DV is an independent adverse marker in fetuses with normal NT.

Methods: This was a prospective study of 163 consecutive patients undergoing NT screening. We considered normal DV, if blood flow in wave A was antegrade and abnormal DV, if it was absent or reversed. In cases of abnormal DV we performed biopsy of chorionic villi or amniocentesis.

Results: In 9 cases there was found an abnormal DV flow (5 aneuploidies, 1 gastroschisis, 1 ascites and extension of extremities due to neuroinfection, 2 normal karyotypes and healthy babies after birth). Among 5 cases of aneuploidies there were 3x trisomy 21, 1x trisomy 18, 1x trisomy X. Abnormal NT was found only in 3 cases of trisomy 21. Normal NT and abnormal DV was found in 6 cases, 4 of them with aneuploidy (trisomy X, trisomy 18) and structural anomalies.

Conclusions: According our results DV sensitivity in chromosomal aneuploidy finding is 100 %, specificity 98,7 %, positive predictive value 71,7 % and negative predictive value 100 %. Abnormal DV appears to predict adverse outcome independently of normal NT. These patients need detailed second ultrasound screening, detailed fetus echocardiography in second trimester and follow-up.

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The prediction of adverse neurodevelopment outcome after perinatal asphyxia using cerebral color doppler ultrasonography

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Objective: The use of color Doppler ultrasonography (cD-USI), allowing simultaneous examination of parenchymal and vascular cerebral structures. The evaluation of blood flow velocities in cerebral arteries is important in assessment of cerebral circulation in hypoxic-ischemic brain damage in neonates. Aim of this study is to assess prognostic cD-USI after perinatal asphyxia in near term neonates.

Methods: 40 term neonates were enrolled prospectively when they had evidence of perinatal asphyxia (Apgar score \( \leq 7 \) at 5min, or cord arterial pH 7.20 and BE>10). Each enrolled neonate underwent neurological examination (after birth, 5 days and on discharge) using a modified Sarnat staging system and simultaneous measurement values of cerebral blood flow velocities (CBFV) and Doppler indices (PI and RI) in anterior cerebral arteries (ACA) during the first 72h of life. Abnormal outcome defined as persistent moderate to severe encephalopathy or neonatal death. We excluded from analysis values of CBFV within 1h of anticonvulsant administration.

Results: Abnormal outcome occurred in 8 (20%) neonates: none of 20 neonates with initial Sarnat stage 1, 5 (29.5%) of 17 neonates with initial stage 2 and in all 3 neonates (100%) with initial stage 3 encephalopathy. The early CBFV (first 12h) was abnormal in 15 (37%) neonates (4 with initial stage 1, 8 with initial stage 2 and 3 with initial stage 3 encephalopathy). After 72h CBFV was abnormal in 6 (15%) neonates (none with initial stage 1, 3 with initial stage 2 and all with initial stage 3 encephalopathy) PSV and specially EDV were significantly lower whereas RI was significantly higher (p<0.05) in severe encephalopathy in first 12h. After 24h PSV and specially EDV increase whereas RI decrease. Conclusion: cD-USI could be very useful for predicting adverse neurodevelopment outcome after perinatal asphyxia. Persistent abnormal CBFV had a better predictive value than early abnormal CBFV.

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Diagnosing ROM: A comparison of the gold standard, indigo carmine amnioinfusion, to the rapid immunoassay, the AmniSure® ROM test

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Objective: To evaluate the potential of the AmniSure® ROM Test to diagnose rupture of membranes by comparing its performance with that of indigo carmine intra-amniotic injection in patients suspected of ROM.

Study Design: A prospective study was conducted. Women presenting to the labor and delivery unit with clinical suspicion of ROM (24 to 42 weeks of gestation) were invited to participate in the study. The study was approved by the IRB and all patients provided written informed consent. Patients were evaluated by sterile speculum examination (pooling, nitrazine and ferning), ultrasound and the AmniSure® ROM Test. The AmniSure® ROM Test was performed before and after indigo carmine injection. Two investigators participated in the clinical assessment. One investigator conducted the two AmniSure® ROM Tests and the other standard tests. A second investigator evaluated the results of the indigo carmine test. A third investigator compiled the results and performed data analysis.

Results:

Conclusion: Results of the AmniSure® ROM Test completely agree with those of the indigo carmine test. These results suggest that a positive AmniSure® ROM Test is as reliable as the injection of indigo carmine for the diagnosis of ROM.

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Patient safety in obstetrics

Gerhard H. A. Visser (The Netherlands)

Regarding intrapartum fetal monitoring normal or severely abnormal fetal heart rate traces are generally adequately recognized. However, many traces are less clear to interpret and clinicians tend to ignore warning signals despite clear guidelines. This requires better training and 24 hour presence of highly qualified specialists at the labour ward and not only the most junior doctors and midwives. The problem of intrapartum fetal monitoring is more a problem of the “boys” than of the “toys”.

Nicklas Dahlström (Sweden)

The aviation industry has for long been considered as being at the forefront with efforts to improve safety. This presentation will explore and compare how concepts from aviation safety may be of relevance also for medicine. An important aspect of such a comparison is the long-standing efforts in aviation of using Crew Resource Management training and simulation for training of crew. The use of simulation for training in medicine may however be over-focused on technical skills. An example of how mid-fidelity simulation can be used to train group interaction and decision making will be presented. Overall conclusions of a comparison between aviation and medicine is that training in context-specific environments needs to be complemented by use of Crew Resource Management training and mid-fidelity simulation for effective competence development.

Isis Amer-Wahlin (Sweden)

In health care the list of mistakes that each clinician accumulates is probably a complex function of length of time in practice, situational factors, individual characteristics, and random chance. Improving safety implies ensuring that individuals and the teams within the organizations learn from the errors they make. Safety in health care combines compassion for patients with concern for practitioners, recognizing that, at a deep level these two are inextricably linked and have the same goal: Evidence based medicine.

Lisa Miller (USA)

Healthcare decision-making is a complex process and errors can be detrimental to patients, families, and clinicians. Cognitive bias can result in poor decision-making, yet few clinicians are aware of the variety of cognitive errors that can impact patient care. Several types of cognitive bias will be explored, with strategies for reducing the impact of bias on clinical decision-making.
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