

nancy, too. Mothers included in methadone program have better prenatal care and lead less risky lifestyle in comparison with heroin-using women. Infants have higher delivery weight and lower incidence of intrauterine growth retardation. Methadone cumulates in liver, lung and lungs of the fetus. After interruption of the umbilical cord methadone is released from deposits in fetal organism. The higher the substitutional dosage at the mother is, the more intensive the withdrawal symptoms are at the infant. Here is described thrombocytosis, higher thrombocytes aggregation activity and systolic hypertension appearing about second week of life and lasting to the 12. week. There are also described sleep cycles disorders, uneasy sleep and abnormalities in REM sleep records. About lactation during methadone therapy there are not uniform opinions. Buprenorphine seems to be the substance that with its characteristics fulfils the basic requirements for substitute treatment of opioid dependence. After discontinuation of the therapy at adults there are minimal withdrawal symptoms. Buprenorphine could replace methadone in elimination of neonatal opioid abstinence syndrome after delivery, when prolonged abstinence syndrome is the main disadvantage of methadone treatment during pregnancy. Buprenorphine was developed as a preparation Temgesic for pain treatment. Preparation Subutex was developed later, after discovery of the possibility of using buprenorphine for detoxification and drug abuse treatment. Buprenorphine is a semi synthetic opiate evolved from thebaine, one of opium components. As a partial agonist buprenorphine has high affinity to mu (μ) receptors, by means of this incites high analgetic effect. Nevertheless, it brings out euphoria too, but in significantly lower level than full agonists. This effect is used in the substitute treatment. Thanks to its partial agonistic effect the intensity of withdrawal symptoms is not so strong as if using antagonists. Buprenorphine is not provably embryotoxic or teratogenic. A content of buprenorphine in the maternal milk does not lead to its refection. No convincing data about its cancerogenic or mutagenic activity or any other genetic risks have been found. Conclusion: Substitutional treatment during pregnancy is very welcomed. It leads to maintenance of stable levels of known drug in organism. As far the drug levels does not fluctuate, the placental insufficiency does not develop and repeated distress of fetus with development of IUGR is eliminated. The risk of sudden fetus death in utero is decreased. Currently the pregnant is resocialized, the antenatal care is improved, the lifestyle changes towards less risky ways. Therefore it is necessary to seek for new substances suitable for substitutional treatment, in particular these ones with low toxicity, low addictive effect, and high affinity to opiate receptors and long terming effect and to use these substances for drug addiction treatment also at pregnant women.

NON-INVASIVE TECHNIQUES FOR PRENATAL DIAGNOSIS AND THERAPY

THE USE OF LOW-MOLECULAR HEPARIN FOR THE PREVENTION OF OBSTETRIC COMPLICATIONS IN WOMEN- CARRIERS OF THROMBOPHILIAS

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Objective: To evaluate the use of low-molecular-weight heparin (LMWH) for prophylaxis in women-carriers of thrombophilia who had suffered from some obstetric complications in their previous pregnancies. **Materials and methods.** We studied 15 women who had an index pregnancies complicated by early severe preeclampsia, abruptio placentae, intrauterine growth retardation or intrauterine fetal death. Subsequently all were diagnosed as carriers of thrombophilias (Factor V Leiden, Prothrombin G20210A mutation, 4G/4G polymorphism of the plasminogen activator inhibitor). LMWH 0,3 ml/daily (Fraxiparin) was administered in their subsequent pregnancy and was started at 7 weeks of gestation. **Results.** Low-molecular-weight heparin was well tolerated and none of the women developed any complications. Only one woman developed obstetric complication. The mean gestational age and the mean birth weight at delivery in the treated group were higher, compared respectively to that in the previously complicated pregnancies without treatment ($p < 0.005$). **Conclusions:** Women with previous obstetric complications and carriers of thrombophilias are more likely to have favourable pregnancy outcome in subsequent pregnancy when treated with LMWH.

of study was to compare the level of endothelial e-selectin and V-CAM, as markers of inflammatory reaction, among pregnant women with PIH, chHT and healthy women (without this complication). Material and method: the study group (SG) considered 47 pregnant women suffered with hypertension (3 with chHT, 16 with PIH, 6 with GDM + chHT, 11 with GDM + PIH, 2 with PGDM + chHT and 9 patients with PGDM + PIH). Control group (CG) consisted of 9 pregnant healthy women, age 23-33. The blood was taken up during the third trimester of pregnancy (29-34 week). Concentrations of soluble selectins and V-CAM were determined with enzyme-linked immunoassay (ELISA). The level of the tension as a standard was the level of "severe hypertension": >160/110 mmHg. The following parameters were registered in both groups: patient's age, the time and mode of delivery, newborn's weight, LGA and hypotrophia occurrence. Also the value, treating and time of diagnosis of hypertension were analysed in SG. The data collected were compared between the SG and CG, using Mann-Whitney's, Chi₂ test and ANOVA, with p value <0,05 considered as statistically significant. Results: The average level of selectin in SG was 67,93(SD=54,72), in CG:66,62(SD=62)(p=NS). V-CAM level in SG: 2122,31(SD=1984)vs in CG:744,51(SD=197,88) (p<0,05). Newborn's weight in SG-2420,36 (SD=1096,7)vs in CG-3383,33(SD=478,3) (p<0,001). Gestational age at the time of delivery: SG:35,19(SD=4,90) vs in CG:38,33(SD1,66) (p<0,05). The highest level of V-CAM (3695,33) : at the group of patients with GDM+chHT. The lowest-at the CG (744,5; p=NS). V-CAM level among the group with GDM+PIH (2170,49) vs patients with GDM+chHT (3695,33) - p<0,05. V-CAM level in patients with hypotrophic newborns(3135)vs eutrophic newborns (1567):p=NS. The highest level of selectin: at the group with GDM+chHT (98,03). The lowest -patients with isolated chHT or PIH (p=NS). E-selectin level in patients with LGA newborns (88,32) vs eutrophic newborns (52,76): p<0,05. Conclusions: Both in pregnancy complicated by hypertension and by DM we observed increased level of adhesion molecules in comparison with the CG. This suggest different degree of endothelial dysfunction among patients with these complications. We found significant increase in VCAM-1 level in the patients who delivered hypotrophic newborns, that may indicate this molecule as a marker of fetal growth inhibition. We found statistically significant increase in sE-selectin level in the group of pregnant women who delivered LGA newborns that suggest that this molecule can be considered as a useful marker of excessive fetal growth. The endothelial dysfunction was the most prominent in pregnancies which coexistence of GDM and chHT.

NON-INVASIVE TECHNIQUES FOR PRENATAL DIAGNOSIS AND THERAPY

LIPID PROFILE CHANGES IN PREGNANCIES COMPLICATED WITH PREECLAMPSIA

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Lipid profile changes in pregnancies complicated with preeclampsia. Some typical changes in the lipid profile are observed which are

more substantial in the first half of normal pregnancy. There is 50% increase in total Chel concentration and 2-3 fold increase of Tg levels. This is explained by reduced tissue LPL activity. In pregnancies complicated with preeclampsia these changes are more pronounced due to suspected impairment of transplacental transport of the cholesterol rich dense LDL particles. The purpose of the study was to compare the serum levels of Chol, Tg, LDL, HDL and VLDL in healthy pregnant women and preeclamptic patients. To examine whether lipid profile in preeclampsia becomes of „atherogenic“ type (i.e. elevated LDL/HDL ratio). To test is there a correlation between the elevation of the total cholesterol and other lipid fractions and the increase of protein loss. Description of project: 31 pregnant women - 17 with preeclampsia (group1) and 14 healthy term pregnant controls (group2) were enrolled in the study. The inclusion criteria for group1 were RR 140/90mmHg and proteinuria over 0.3g/24h. The exclusion criteria were any underlying systemic, vascular or renal disease. Fasting blood samples were used for evaluation of plasma levels of Chol, Tg, LDL, VLDL and HDL and also for the standard biochemical tests. Protein excretion in 24 hours protein samples was estimated. Results: Chol, Tg and LDL were significantly higher than the recommended by the WGCVD in both groups. In preeclampsia this elevation was more pronounced /p<0.05/. The mean LDL/HDL ratio in group 2 was lower than in group 1 which predicts a possible low atherogenic risk in healthy pregnant women compared to a suspected moderate to high atherogenic risk in patients suffering from preeclampsia /p<0.05/. There was a positive correlation between the increase of the protein loss and the elevation of the Chol and Tg levels in group 1/p<0.05/. Conclusions The results obtained in our preliminary study don't validate the hypothesis whether lipid profile changes during pregnancy are result of or cause for some of the pathophysiologic changes observed in preeclampsia. Some preventive protocols could be offered to women with high atherogenic risk detected in previous pregnancy.

SUPRASELECTIVE VASODILATOR THERAPY IN PREECLAMPSIA

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In the last 15 years several worldwide scientific groups consistently reported the existence of LH receptors in extragonadal sites. The most astonishing location was found to be in the vascular smooth muscle layers of uterine and spiral arteries. Subsequent studies using doppler measurement revealed that hCG administration in first trimester pregnancies was followed by decreasing of uterine artery resistance index.

Objective: The aim of the current workout is to establish the effect of hCG vasodilator effect by pulsatile hCG administration in cases of pregnancies complicated with preeclampsy.

Material and Method: study design: prospective, nonrandomised study. Inclusion criteria: pregnant women with PIH and clinical or paraclinical signs of preeclampsia. Exclusion criteria: documented

patients with high AS. Also, within the first group, increased frequency of various prenatal stress conditions was registered, but statistical trial (Fisher exact test) didn't confirm statistically significant difference ($p > 0.05$) in intensity of mentioned conditions between two groups. Also, measured serum cortisol levels were evidently higher in all neonates which were affected by any kind of prenatal stress, beside asphyxia. Yet, comparative analysis of those variables (MANOVA) didn't reveal statistical significance.

DISCUSSION: Obtained results clearly show birth asphyxia is significant and strong inductor of stress in newborns. Other reported results, point to conclusion that stress may be accumulated and that intensity of adrenal response depends on quantity of stress. When asphyxia was present, lower increase of cortisol has been registered in neonates who have been exposed to prenatal stress factors, probably because repeated and/or prolonged stress has led to certain exhaustion of suprarenal glands. As adequate adrenal response is essential for survival, those neonates might be in unfavorable situation. These findings are in accordance with results of other authors who have conducted similar studies. **CONCLUSIONS:** Fetus should be treated as a patient, even when we are dealing with stress. Adequate treatment and prevention of various pathological disorders should be provided in order to decrease fetal stress, creating better conditions for sufficient synthesis of fetoplacental hormones and proper adrenal response at the birth and/or when additional stress is present.

DIABETES IN PREGNANCY

SELEN AND GLUTATHION PEROXIDASE ENZYME LEVELS IN DIABETIC PATIENTS WITH EARLY SPONTANEOUS ABORTIONS

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The incidence of spontaneous abortions in women with type 1 diabetes mellitus varies between 10-30%. The etiology of this is still unclear despite numerous experimental studies. Pregnancy is a condition of increased oxidative stress due to impaired balance between pro- and antioxidants. Glutathion and related enzymes perform the best antioxidant protection. Some authors point to a possible correlation between spontaneous abortions and low plasma Se levels as well as low intracellular activity of glutathion peroxidase enzyme. Others report that Hb A1_c values over 1SD above normal increase the risk of spontaneous abortions with 3% and Hb A1_c values between 10-12% are critically high for the occurrence of spontaneous abortions. The purpose of the study was to evaluate the levels of Se and glutathion peroxidase enzyme (G1-Px) in pregnant women with type 1 diabetes mellitus in the first trimester of pregnancy and to find out if there is a correlation between glycemic control of diabetes and the incidence of spontaneous abortions. Description of project 75 pregnant women enrolled in an- 1 year prospective study divided in 3 groups according to pregnancy outcome: gr.1-n=30 with type1 diabetes mellitus, no abortions, gr.2-n=16 with type1 diabetes mellitus with first trimester spontaneous abortion and gr. 3-n=29 healthy pregnant women. Women with type1 diabetes melli-

tus were divided into three subgr. according to glycemic control _ subgr.1- n=12(_b A1_c < 7%), subgr.2 _ n=18(_b A1_c > 7< 8%), subgr.3-n=16(_b A1_c > 8%). G1 _Px activity was determined in Et hemolysate with test reagents of Randox Ransel, with ref.values 27.5 _ 73 U/g Hb. Selen concentration was determined in whole blood sample by atomic absorption spectrophotometry with ref.values 0.12-1.1 _mol/l. Hb_{1c} was measured by affinity chromatography with ref.values 4.5 _ 6.3%. Statistical methods used were: dispersion, correlation analysis - SPSS package version 11.01.01. Results Basic Se levels were low in all pregnant women in early pregnancy. The metabolic control level did not influence the levels of Se in pregnant women with diabetes mellitus type1. G1 -Px activity was within the normal limits in all women. There was no correlation between Se levels and G1 -Px activity in pregnant diabetics with and without abortions. There was a correlation between Se levels and G1 -Px activity only in healthy pregnant women. Pregnant women with poor glycemic control had higher incidence of spontaneous abortions. Table. Gt - Px activity according to glycemic control _b A1_c < 7% _b A1_c > 7< 8% _b A1_c > 8% Women with no abortionsn = 9 (30%) Women with abortionsn = 3 (18.7%) Women with no abortionsn = 14 (46.6%) Women with abortionsn = 4 (25%) Women with no abortionsn = 7 (23.4%) Women with abortionsn = 9 (56.2%) PrePr - G1 6.0 ± 1.84P=0.04 6.6 ± 0.05 7.6 ± 0.07P=0.3 7.55 ± 0.81 5.45 ± 1.5P=0.007 7.44 ± 0.71 Hb A1_c 6.5 ± 0.2P=0.03 6.6 ± 0.15 7.7 ± 0.21P=0.3 7.47 ± 0.35 8.65 ± 0.38P=0.02 9.26 ± 0.59 Gt - Px 42.6 ± 12P=0.89 41.3 ± 13 35.1 ± 14.1P=0.2 41.5 ± 1.85 43.1 ± 12.5P=0.7 41.4 ± 8.94 Conclusions We could not support the hypothesis of reduced antioxidant protection (low Se and Gt _ Px levels) as a causative factor in the pathogenesis of spontaneous abortions in diabetic patients. Our study results showed that poor metabolic control of diabetes (high Hb A1_c) in the first trimester of pregnancy had a primary role in the occurrence of early abortions. We could speculate that the early hyperglycemic maternal-fetal environment most probably plays a role of an additional stress to the developing embryo.

NEW TECHNOLOGIES IN PRENATAL CARE

INDUCTION OF LABOR AT TERM IN DIFFERENT REGIMENS

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Introduction: The induction of labor is a common practice in obstetrics to avoid the maternal and neonatal risks of continuing the pregnancy. During last decade new induction methods have been introduced.

Objective: The purpose of this study was to compare the efficacy and safety of different regimens for induction of labor at term, practiced in Tartu University Women's Clinic, Estonia during recent years. **Study design:** The two regimens of induction of labor were evaluat-

onal genotype could differ depending on whether the T-allele is of paternal or maternal origin (parent-of-origin effect). The aim of this study was to evaluate these effects by means of applying several tests and techniques. Data on 105 children with spina bifida, a type of NTD, and their parents were available. The 76 complete parent-child triads were analysed using the transmission disequilibrium test (TDT), the transmission asymmetry test (TAT), and a log-linear model with likelihood ratio tests. The TDT showed a preferential transmission of the T-allele to NTD children but was not significant (Chi-square 2.12; $p=0.09$). The TAT pointed towards an influence of a maternally derived T-allele (Chi-square 3.32; $p=0.07$). The log-linear model demonstrated an embryonal genotype effect and a significantly higher risk for a maternally versus a paternally derived T-allele. The relative risk (95% CI) estimates in the full log-linear model for the CT versus the CC child genotype were 0.8 (0.3-1.9) and 2.6 (1.1-6.0) for a paternal and maternal T-allele, respectively. The application of several methods of analysis showed that the relation between MTHFR 677 genotype and NTD seemed to be mediated through a maternally derived T-allele. However, the results were inconclusive and preliminary analysis of additional incomplete triads pointed towards the presence of a maternal effect through intrauterine environment.

PI39

HOMOCYSTEINE LEVELS IN NORMAL AND PREECLAMPTIC PREGNANCIES

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Endothelial dysfunction is claimed to be a leading cause of development of preeclampsia. The mechanism of the endothelial activation remains unclear for now. A number of predisposing factors are discussed. One of them is homocysteine as a known endothelial damage activator.

In our study 27 pregnant women were included: 15 with preeclampsia (group 1) and 12 healthy term pregnant women (group 2). They were admitted to the Maternal Risk Clinic between December 2003 and August 2004. Only singleton pregnancies without fetal malformations were included. The inclusion criteria were $>140/90$ mmHg and proteinuria over 0.3 g/24h. Six of the women had a superimposed preeclampsia - 3 patients had diabetes, 2 - nephrolithiasis and 1 M. Basedowi. Two of the women were developed preeclampsia in a previous pregnancy.

The mean homocysteine level in the group1 was 11.01 $\mu\text{mol/L}$ and 6.24 $\mu\text{mol/L}$, in the group2 ($p<0.05$). Of all preeclamptic women only one (0.6%) had a serum homocysteine level lower than the mean for the group2. The women with a severe form had a significantly higher serum homocysteine levels than those with mild preeclampsia ($p=0.025$). In 8 patients pregnancy was terminated before 34 weeks of gestation. Eight of the women delivered fetuses with low and extremely low birth weight.

In 6 of the women without accompanying disease a DNA analysis for inherited thrombophilia was made. One of them was homozygous for Factor V Leiden, one for C677T MTHFR and one was heterozygous for the same mutation of MTHFR. In 3 cases no mutations were estimated.

Our data show a significant difference between the mean levels of homocysteine in normotensive and preeclamptic patients and also between the mild and the severe forms of the disease. The results show a link between the serum

homocysteine levels and the development of preeclampsia. The results also support the hypothesis of a positive connection between the severity of the preeclampsia and the elevation degree of the homocysteine levels.

PI40

PLASMA HOMOCYSTEINE, VITAMINE VALUES AND ANTIEPILEPTIC THERAPY IN PREGNANCIES WITH NEURAL TUBE DEFECTS

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In pregnancy, a part folate deficiency, another acquired fetal neural tube defect (NTD) risk factor is antiepileptic therapy. Valproic acid (VA) has adverse effects: antifolate activity, alterations in the homocysteine cycle and a reduction in plasma vitamin B6. We report the cases of 4 women: MT, LC, NM, CA, with VA therapy, with a NTD affected offspring, even under 5 mg/day folic acid complement. Their results were compared with those of a woman, under VA, CW, and of 57 pregnant women, all with a normal pregnancy. Plasma homocysteine (Hcy), folate, vitamins B12, B6, and red cell folate levels were measured in samples. Some mutations were sought, involved in Hcy metabolism, linked with the folate metabolism: C677T (MTHFR gene), A2756G (MTR gene), A66G (MTRR gene), and codon 259 (TCII gene).

Results. the cases reported showed B6 decreased values, as another woman, CW, under VA, but with a normal pregnancy. However, under folic acid complement, plasma and erythrocyte folate values were lower in MT, CA, as in NM, than in CW and even than in LC. That might showed a trouble in the folate or in the homocysteine metabolisms, even if no hyperhomocysteinemia was seen (the subjects received folic acid supplement). In the cases, two heterozygote mutations were observed. CW, with a normal pregnancy, showed higher plasma and erythrocyte folate values than the cases and a sole heterozygosity. Vitamin B6 deficiency decreased nicotinic acid synthesis from tryptophane, and so, decreased NAD⁺ and NADP⁺ synthesis, necessary to pyrimidine nucleotide synthesis. NTD are multifactorial diseases. In the cases, the association of a B6 vitamin decrease, due in particular to the therapy, with an unfavorable genetic profile, could be responsible of NTD. MT, with a periconceptional pyridoxine therapy, had a normal pregnancy, and a healthy child.

PI41

PREDICTORS AND EFFECTS OF FOLATE SUPPLEMENT USE: THE NORWEGIAN MOTHER AND CHILD COHORT STUDY

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Aims. The objective of this study was to investigate differences in prevalences of some life style factors and demographic parameters between folate supplement users and non-users in a large ongoing cohort study of Norwegian

P13. IMMUNE THROMBOCYTOPENIC PURPURA AND PREGNANCY OUTCOME

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Introduction: Immune thrombocytopenic purpura (ITP) occurs in 1 to 2 every 1000 pregnancies; the risk of maternal and fetal complications is enhanced and additional monitoring and therapy may be needed. None of the mother's clinical or biological parameters and no antenatal measures reliably predict fetal/neonatal status.

Material and Methods: Eleven pregnant ITP patients were observed between March 2000 and January 2005. The main haematology parameters, bone marrow aspirates, platelet antibodies, anticardiolipin and antinuclear antibodies, and serum thrombopoietin level were investigated in an experienced laboratory.

Results: The mean age was 28,(54); two of our patients were pregnant for the second time, and previous neonatal outcome predicted the normal neonatal platelet count in the subsequent pregnancy. The ITP was known in 10 patients and splenectomy was carried out before pregnancy in 2 patients; in one case the ITP was discovered in the 11th weeks of gestation. Maternal therapy with IvIgG and steroids was given antenatal and continued during post-partum period in 9 cases. One newborn had a transitional thrombocytopenia and another offspring of a woman with previous splenectomy had platelet count 28.109/L; transfusion of random platelets combined with perfusion of polyclonal immunoglobulins (IvIgG) for 2 days, prevented ICH in the second case.

Conclusions: ITP in pregnant women can induce moderate or severe thrombocytopenia in the fetus or neonate; although pregnancy is not discouraged in women with preexisting ITP, there is a major risk of fetal bleeding and intracranial hemorrhage.

P14. A RARE CASE OF ASYMMETRIC LOWER LIMB REDUCTION DEFECT DETECTED BY ULTRASOUND IN THE SECOND TRIMESTER OF PREGNANCY

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Abstract Text: Congenital limb reduction defects (LRD) are rare abnormalities. The incidence is estimated to be 0.54 to 0.59/ 1000 live-born infants. Additional anomalies are present in over one-half of the cases and the limb defects may be part of a chromosomal abnormality. The exact pathogenetic mechanism for the development of this defect is unknown. We present a case of an isolated terminal transverse LRD in a second trimester fetus diagnosed in the course of a routine anomaly scan examination in a low risk patient. There was an association with hypoplastic left heart syndrome and medullar renal dysplasia. The karyotype proved to be normal 46, XX. After counseling the parents decided pregnancy termination. Detailed ultrasound examination of the fetus allows early diagnosis of the defect and helps the couple in their decision regarding the fate of the pregnancy.

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Abstract: Even though presumably identical twins, arising from
tilized ovum, sharing the same genetic material and exposed to the
ment in the uterine life, we present a situation of striking morpholog
as between such twins. Maternal and method A 37 years old woman,
/ of 7 spontaneous first trimester abortions, presents at emergency
inal bleeding and low abdominal pain during the last 2 days after 8
norrhoea. The ultrasound scan diagnosed a monochorionic, monam
egancy and after allaying the bleeding, a cervical cerclage was per
shortened cervix, 1 cm open) and close observation decided. Results
uchal translucency is measured in both embryos, showing normal val
first alarm sign is drawn when cranial structure of one twin, situated
of the uterine cavity, is not properly visible, too soon though, to
agnosis. The scan performed at 16 weeks GA shows the first twin
ore or less as expected, whereas the second twin has no identifiable
structure. Amniocentesis and the cytogenetic analyses found no cro
omalities. At 18 weeks GA the ultrasound scan shows no sign of car
the anencephalos twin, as well as an increasing delay in morpholog
ent of both twins, followed two days later by the death of the other
: Obviously, the development of the fetuses in a monozygotic preg
rmed by the genetic factors and environmental conditions, but it
are more subtle elements that can modify this evolution and have
to consideration.

TAL ORIGIN OF BRAIN DAMAGE

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n widely referred as "birth asphyxia" occurs as a result of hypoxia-
ng the process of delivery. In full term infants it is still an important
eurological disability and long term handicap. The aims of our study
it the incidence of birth asphyxia and consequent hypoxic-ischaemic
y (HIE) and to correlate the depth of birth asphyxia and severity of
1 infants.

d methods: we investigated the full term infants born at
ecology Clinic in Skopje, Macedonia during 2003 and 2004. We used
rotocol and scoring system for diagnosis of birth asphyxia, and for
IIE Sarnat&Sarnat classification in three grades.

g the investigated period there were 6432 full term infants. The inci-
asphyxia was 14,3/1000 liveborn fullterms (92/6432). The inci-
birth asphyxia was 9,6/1000 fullterms and for severe birth asphyx-

HIE 14,3/1000 liveborn infants. There was high coefficient of correlation
between the severity of birth asphyxia and grade of HIE ($r=0,72$).
Conclusion: It is very important to detect the early prepartal signs of intrauterine
hypoxia and to prevent birth asphyxia, because of its high correlation with the con-
sequent HIE and the risk for known longterm disability

P29. NEONATAL EARLY ONSET SEPSIS AND ITS CORRELATION WITH MATERNAL RISK FACTORS

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Abstract Text: Neonatal Early onset sepsis(EOS) in newborns is not very common
in ordinary neonatal units, about 1-4/1000 liveborns, but in Neonatal intensive
Care units it is much more frequent, over 4-10/1000 liveborns, and for premature
infants over 6%. The incidence depends on the type of nursery and on conditions
predisposing to infection(maternal, environmental, and host factors). Our aims
were to present the incidence of EOS at Department of neonatology within Obstet-
ric&Gynecology Clinic in Skopje, Macedonia and to correlate it with known mater-
nal risk factors for infection.

Material: newborns born on O&G Clinic during a two years period, 2003 and
2004. It was a prospective study, method used: clinical, biochemical, microbiolog-
ical, statistical.

Results: during the examined period there were 8313 newborns. EOS was con-
firmed in 27 newborns, 24 premature (88,9%) and 3(11,1%) fullterm infants. The
overall incidence was 3,2/1000 liveborns. In the NICU the incidence of EOS was
9,3/1000 admissions. There was statistically significant difference ($P<0,05$)
between the frequency of EOS in premature and fullterm infants. As known mater-
nal risk factors for infection were evaluated: chorioamnionitis (8/27), premature
rupture of the membranes(14/27), maternal fever (or other biological signs of
infection) (6/27), urinary tract infections (5/27). Some of the babies had more than
one risk factors. Rodwell score for diagnosis of sepsis was performed, combined
with clinical signs and microbiological confirmation. The prevalent microorganism
in EOS was staphylococcus coagulasa negative (63%).

Conclusions: our results are in accordance with literature data, but they imply the
continuous need for improving antenatal and perinatal care in order to prevent all
preventable risks for neonatal/perinatal infections, because the premature infants
are very susceptible for infections and infection is a very important cause of death.

P30. FREQUENCY OF MINOR AND MAJOR FETAL MALFORMATIONS IN DIABETIC PATIENTS WITH HIGH INITIAL LEVELS OF HB A1C IN EARLY PREGNANCY

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Abstract Text: The aim of the study was to evaluate the correlation between

tion from the procedure was relief from anxiety (88/100); the commonest expectation expected to have fetal abnormalities excluded (76/100) and estimated date of delivery confirmed (59/100). They also reported that they just wanted to have a visual contact with the fetus (68/100), sex confirmation was also desirable (70/100), whilst harmless for the fetus (77/100). In case of detection of a fetal abnormality 59 out of 100 women would opt for termination of pregnancy, 15 (76/100) believed that the particular ultrasound scan's accuracy exceeds 50% and 44 out of 100 women believed that accuracy exceeds 75%.

Conclusions: Most women were informed of the benefits and limitations of the second trimester Level II ultrasound scan. There is still place for further patient education on obstetric ultrasound scan.

O13. MULTIFETAL PREGNANCY REDUCTION

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Introduction
High order multifetal pregnancy is a common problem, as a result of assisted reproduction techniques. There are considerable risks for mother and fetuses and high economical costs. The selective reduction of the fetal number has become an option.

Material and methods
Nearly 150 multifetal pregnancies have undergone selective reduction in the last years. The procedure was performed with intrathoracic KCL injection, at 11 - 13 weeks gestational age. The results and conclusions of this series will be presented.

O14. NUCHAL TRANSLUCENCY SCREENING FOR FETAL CHROMOSOMAL ABNORMALITIES AT 11-14 WEEKS GESTATION

Dimitrova V.¹, Markov D.², Chernev T.¹, Karagyozova Zh.¹, Mazneikova V.¹
¹ State University Hospital "Maichin Dom", Department of Obstetrics and Gynecology, Medical University, Sofia, ² Department of Medical Genetics, Medical University, Sofia

Aim: To assess the feasibility of nuchal translucency (NT) screening for Down syndrome (DS) and other chromosomal anomalies (ChA) between 11-14 weeks of gestation [w.g.].

Material and methods: A longitudinal prospective follow up study was carried out at a tertiary referral center including 408 singleton pregnancies between 11+0 and 14+0 w.g. Three experienced sonographers performed transabdominal and/or transvaginal scanning with high resolution ultrasound equipment. The ultrasound examinations included assessment of fetal number and viability, NT measurement and fetal anatomy survey. DS risk was calculated using the computer program of

The Fetal Medicine Foundation, UK. Invasive prenatal diagnosis was offered whenever the estimated DS risk was $\geq 1/300$. Follow up scans were scheduled as appropriate, including fetal echocardiography. Pregnancy termination was an option in cases of affected fetuses. Pregnancy outcome was ascertained from hospital records, referring physicians or the patients themselves.

Results: 108 (26%) out of the 408 women were ≥ 35 years and the rest were below that age. 9 fetal ChA were found in total, including 6 cases with DS, 2 with trisomy 18 and 1 with monosomy 45,XO. The overall sensitivity for DS was 66.7% and for all ChA - 77.7%. The overall sensitivity and false positive rate for ChA for patients ≥ 35 years was 80% and 35%, while for patients < 35 years it was 66.7% and 5.1%, respectively. Diagnostic invasive procedures were performed in 50 out of 56 screen-positive cases, including 7 of the cases with ChA. In all these 7 cases pregnancy termination was performed.

Conclusions: First trimester NT screening for DS has high sensitivity and specificity. Its other potential advantages include screening for chromosomal abnormalities different than DS, early prenatal diagnosis of major structural anomalies, screening in multiple gestations and earlier and safer termination of affected pregnancies.

O15. DOWN'S SYNDROME DETECTION BY TRIPLE TEST

Athanasiou E., Bradley R.

Obstetric department, Royal Sussex County Hospital, Brighton, England

Introduction: To find out the detection rate of Down's syndrome by the use of triple test in combination with ultrasound scan in our department, which is tertiary referral center.

Material: Revision of total number of 25,906 triple tests during the period of approximately 6 years (1/1/91 to 25/3/97).

Results: There were 1266 women with increased risk of Down's syndrome (4.8%) of Down's. The total Down's syndrome cases were 79 (6.2%), 32 detected by triple test, 9 missed by triple test. 19 women had no triple test done, 14 were detected by amniocentesis or chorionic villus sampling (CVS), and 5 were detected by nuchal translucency or the 20 week scan.

Conclusions: The detection rate of triple test for Down's syndrome is 78% in women of age 37 or older demand for invasive prenatal diagnosis. There are still women who either miss, forger or don't do the triple test. If a woman has an increased risk from the triple test the possibility of the baby to have Down's syndrome is 6.2% and in a woman with a negative triple test the possibility is 0.03%.

O16. REFERENCE RANGE FOR FETAL NASAL BONE LENGTH AT 11-13+6 WEEKS GESTATION IN A GREEK POPULATION

Benardis P., Pilalis A., Souka A., Antsaklis A.

Alexandra General Hospital, Fetal Medicine Unit, 1st Department of Obstetrics and Gynecology, University of Athens, 'Alexandra' General Hospital, Athens, Greece

Abstract Text: Introduction The aim of this study was to provide a reference range for the length of the fetal nasal bone at 11-13+6 weeks gestation in a Greek

C4. INHERITED THROMBOPHILIA AND PREGNANCY COMPLICATIONS

Koleva R.¹, Dimitrova V.¹, Savov A.², Mazneikova V.³, Chernev T.¹, Karagyozeva Zh.¹
¹ Fetal Medicine Department, State University Hospital "Maichin Dom", Sofia
² Molecular Pathology Laboratory, State University Hospital "Maichin Dom", Sofia
³ High maternal risk Clinic, State University Hospital "Maichin Dom", Sofia, Bulgaria

Aim: To assess the clinical significance of inherited thrombophilia [IT] for the development of some pregnancy complications.

Material and methods: The incidence of the following factors was studied in 97 pregnant women with pregnancy complications and in 100 controls: Factor V Leiden [FVL] and Prothrombin G20210A mutations, homozygous methylenetetrahydrofolate reductase deficiency [MTHFRD], 4G/4G polymorphism of the plasminogen activator inhibitor [PAI]. Among 97 patients in the group studied 39 had early onset severe preeclampsia [PE], 14 -placental abruption [AP], 8- intrauterine growth restriction [IUGR], 12 -stillbirth [SB], 14- habitual spontaneous abortions [HSA]. The control group included 100 clinically healthy pregnant women with at least one previous uneventful pregnancy, without history of thromboembolic disorders. DNA analysis was performed according to internationally accepted standards. Pregnancy outcomes were ascertained from hospital records. Statistical significance ($p < 0.05$) was assessed by means of Student's t-test.

Results: 64 patients from the studied group (66%) and were carriers of at least one of the mutations/polymorphisms. FVL mutation was found in 24% of the patients from the studied group, Prothrombin G20210A in 11% and PAI 4G/4G polymorphism in 31%. In the control group the frequency of these mutations/polymorphisms was significantly lower - 6%, 3% and 14.5% respectively. Homozygous MTHFRD was not more frequent in the studied group (8.2%) compared to the control one (29%). Eight of the patients (9.6%) were carriers of more than one mutation. In 22 cases with early onset severe PE and IT gestational age and birthweight at delivery were lower than in the cases with severe PE without IT.

Conclusions: Inherited thrombophilia is found more frequently in women with pregnancy complications like PE, IUGR, AP, SB, HSA. The incidence of homozygous MTHFRD is not higher in these cases. The diagnosis of IT is important since antithrombotic therapy has to be considered to protect the mother and the fetus.

O5. HASHIMOTO'S THYROIDITIS AND PREGNANCY; REVIEW OF 30 CASES

Ozyuncu, O.¹; Beksac, S.¹; Basaran, A.¹; Guler, T.¹; Katlan D.¹
¹ Hacettepe University Faculty of Medicine, Hacettepe University School of Medicine, Department of Obstetrics and Gynecology, Ankara, TURKEY

Abstract Text: Introduction and aim: The most common cause of acquired hypothyroidism is autoimmune thyroiditis (also called Hashimoto's disease), which is seven-fold more common in women with increasing incidence during middle life. The role of autoimmunity in its pathogenesis is supported by the histological findings of diffuse lymphocytic infiltration of the thyroid gland and presence of circulating thyroid autoantibodies in almost all patients. Thyroid autoimmunity is thought to be associated with reproductive failure, pregnancy loss, ablatio placentae, IUGR, hypertensive disorders of pregnancy and with poor neonatal outcome. Therefore, the aim of this study is to evaluate the pregnancies with hashimoto thyroiditis.

01. EVALUATION OF HOMOCYSTEINE LEVELS IN PREECLAMPSIA

Stoykova V., Maznejkova V., Ivanov St., Tzontcheva A.
Sbalag "Maichin dom", University Maternity Hospital "Maichin dom", Maternal Risk
Dept., Sofia, Bulgaria

Preeclampsia is one of the most common and severe pregnancy complications, whose etiology remains unclear. It is supposed that endothelial dysfunction may play a key role in the development of preeclampsia. Homocysteine is an important independent cardiovascular risk factor, which might induce the process of endothelial dysfunction. We present preliminary data from a prospective ongoing clinical study, which is carried out in the University Maternity Hospital "Maichin dom". 26 pregnant women - 14 with preeclampsia (group1) and 12 healthy third trimester pregnant controls (group2) were enrolled in the study between December 2003 and August 2004. The inclusion criteria for the group1 were RR \geq 140/90mmHg and proteinuria over 0.3g/24h. Six of the women from group 1 revealed features of superimposed preeclampsia, three of them had concomitant diabetes mellitus, two suffered from nephrolithiasis and one had M. Basedowi, two had developed preeclampsia in a previous pregnancy. The mean homocysteine level in the first group was 11,04 mmol/l ($p < 0.05$), while in the control group it was 6,24 mmol/l ($p < 0.05$). Of all 14 pregnant women from the first group, only one (0.7%) had a serum homocysteine level lower than the mean for the control group. The women with a severe preeclampsia had a significantly higher serum homocysteine levels than those with mild form ($F = 0.025$). Seven of the patients (50%) gave birth before 34th weeks of gestation. Three of the patients had complications such as HELLP syndrome and retinal hemorrhages. The study finds a possible link between the serum homocysteine as an endothelial dysfunction marker and the development of preeclampsia. The results also support the assumption of a positive relation between the severity of preeclampsia and the degree of the elevation of the serum homocysteine levels.

02. THE RELATION OF THROMBOPHILIA AND PREECLAMPSIA

Demir S.C., Evruke C, Ozgunen F.T., Kadayifci O., Altintas U.
Zukurova University, Faculty of Medicine, Zukurova University, Obstetrics & Gynecology Dept. Adana, Turkey

Objective: The aim of this study is to search for a relation between some thrombophilic parameters and preeclampsia.

Materials and Methods: Patients were divided into two groups. Control Group: This group covers 102 normotensive patients who are over 20 weeks of pregnancy without any pregnancy pathologies. Study Group: This group covers 100 patients over 20 weeks of pregnancy with preeclampsia. In all cases: complete blood count, antithrombin III, protein S levels, factor V Leiden mutation, prothrombin 20210 mutation methylentetrahydrofolate reductase 677 mutation and homocysteine levels were studied. Statistical analysis of the data was done by SPSS 11.0 programme. In the comparison of two groups as control and PIH Mann-Whitney U Tests, and the PIH subgroups comparison with each others was done by Kruskal-Wallis Tests. The levels of $p < 0.05$ were accepted as statistically significant. **Results:** Antithrombin III deficiency, protein C deficiency, hyperhomocysteinemia were found to be related with preeclampsia. But protein S deficiency, and homozygote factor V Leiden muta-



СЪЮЗ НА НАУЧНИТЕ МЕДИЦИНСКИ ДРУЖЕСТВА В БЪЛГАРИЯ
БЪЛГАРСКО ДРУЖЕСТВО ПО АКУШЕРСТВО И ГИНЕКОЛОГИЯ

ул. Злате 2, София 1431, Тел. 02 - 51-66-353 Факс 02 - 51-72-71; e-mail: hsobgyn@abv.bg

Posters: PO111 - PO127

Sunday, September 1

8.30-10.00

Plenary Session PS9 Prenatal Diagnosis and Genetic Counselling

Chairpersons: V. G. Voronina, Vladivostok, D. Markov, Antwerpen

- | | | |
|-------------|-------|--|
| 8.30-8.45 | PS55. | RAPID PRENATAL DIAGNOSIS OF COMMON ANEUPLOIDIES BY QUANTITATIVE FLUORESCENT POLYMERASE CHAIN REACTION
S. Arsovska, P. Dimcev, M. Kaeva, G. D. Efremov, D. Plaseska-Karantilska, (Skopje) |
| 8.45-9.00 | PS56. | PRENATAL DIAGNOSIS OF THE MOST COMMON ANEUPLOIDIES IN BULGARIA BY QUANTITATIVE FLUORESCENT PCR (QF-PCR) ANALYSIS
S. Andonova, V. Dimitrova, V. Mazneikova, R. Tacheva, D. Toncheva, I. Kremensky, (Sofia) |
| 9.00-9.15 | PS57. | STRUCTURE PRENATAL DIAGNOSED CHROMOSOMAL ABNORMALITIES IN PRIMORYE TERRITORY
V. G. Voronina, F. F. Antonenko, S. V. Voronin, (Vladivostok) |
| 9.15-9.30 | PS58. | PRENATAL DIAGNOSIS OF LYSOSOMAL STORAGE DISEASES IN BULGARIA- RESULTS FROM 8 YEARS OF EXPERIENCE
Smigerska L. K. Vladimirova I. Simeonov, R. Tacheva, B. Dimitrov, and V. Dimitrova, Sofia |
| 9.30-9.45 | PS59. | CORDOCENTESIS AT 18-29 WEEKS OF GESTATION: EXPERIENCE OF 647 CASES
S. Brankovic - Niksic, S. Nikolic, D. Petrovic, M. Jelisavcic, Belgrade |
| 9.45-10.00 | PS60. | EARLY PRENATAL DIAGNOSIS OF BILATERAL CLEFT LIP ASSOCIATED WITH INCREASED NUCHAL TRANSLUCENCY - A REPORT OF TWO CASES
D. Markov, T. Cherney, Y. Leroy, P. Loquet, (Sofia) |
| 10.00-10.30 | | Coffee break |
| 10.00-11.00 | | |

Poster Session PO9 - Prenatal Diagnosis and Genetic Counselling

Posters: PO128 - PO134

10.00-11.00

Late Posters Session PO10

Posters: PO135 - PO155

11.00-11.45

Workshop Lectur in bioethics
Chairperson V. Ganev



СЪЮЗ НА НАУЧНИТЕ МЕДИЦИНСКИ ДРУЖЕСТВА В БЪЛГАРИЯ
БЪЛГАРСКО ДРУЖЕСТВО ПО АКУШЕРСТВО И ГИНЕКОЛОГИЯ
Posters: PO049 - PO058 София 1431, Тел. 02 / 51-66-353 Факс 02 / 51-72-71; e-mail: bsobgyn@abv.bg

18.00-19.00

Poster Session PO5 - Neurogenetics

Posters: PO059 - PO069

Saturday, August 31

8.30-12.00

Plenary Session PS6 - Monogenic Diseases

Chairpersons: Jean-Pierre Fryns, Leuven, N. Bogdanova, Muenster

- 8.30-9.00 PS30. X-LINKED MENTAL RETARDATION: FROM FRAGILE X SYNDROME TO THE NEW GENES
S. Frints, Jean-Pierre Fryns and the European XLMR Consortium
- 9.00-9.15 PS31. GENETIC SERVICE FOR DIAGNOSIS OF GENETIC DISEASES IN BULGARIA
Kremensky I., A. Savov, S. A. Jordanova, A. Todorova, S. Andonova, B. Georgieva, M. Ivanova, V. Dimitrova, V. Mäznejkova, T. Chernev, A. Dimitrov, R. Petkova, E. Michajlova and L. Kalayjieva. (Sofia)
- 9.15-9.30 PS32. THE FREQUENCIES OF HFE C282Y AND H63D MUTATIONS IN THE POPULATION OF THE REPUBLIC OF MACEDONIA
K. Davcheva, T. Jevtic, R. Mihcevic, D. Plaseska-Karanfilska, A. Dimovski, G. D. Elremov (Skopje)
- 9.30-9.45 PS33. MUTATION ANALYSIS OF THE HFE GENE IN EURASIAN POPULATIONS OF RUSSIA
R. I. Fatkhislamova, L. M. Berdina, C. Fedorova, E. K. Khusnutdinova (Ufa)
- 9.45-10.00 PS34. HAEMOCHROMATOSIS GENE MUTATIONS IN CROATIAN POPULATION
S. Ristić, N. Starčević Čizmarević, B. Brajenović-Mihic, I. Pleša, S. Mihic, D. Štimac, B. Peterlin, M. Kapovic (Rijeka, Ljubljana)

10.00-10.30

Coffee break

Chairpersons: M. Stevanovic, Belgrade, E. S. Sahin, Istanbul,

- 10.30-10.45 PS35. AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): GENETIC AND BIOCHEMICAL ASPECTS
A. Markoff, N. Bogdanova, F. Qian, K. Hackmann, C. Rüffer, B. Dworniczak, J. Horst, B. Nilus, G. G. Gemino, V. Gerke (Muenster, Baltimore, Leuven)
- 10.45-11.00 PS36. SPECTRUM OF CONNEXIN 26 GENE (GJB2) MUTATIONS IN

FC3.17.07

CORRECTION OF SPECIFIC AUTOIMMUNE DISORDERS FOR PREGNANT WOMEN WITH DIABETES MELLITUS

V. Petrukhin, T. Budikina, F. Burumkulova, A. Poletaev, V. Gurieva, N. Volkova, Moscow Regional Scientific Research Institute of OB/GYN, Moscow, Russia

Objectives: As shown in our previous experiments, for diabetic women is characteristic the increased levels of insulin (AT-1) and its receptors (AT-2) antibodies. These antibodies, linking the factor of growth of nerves, conduct to the disturbances in the nervous system of a fetus and newborn. The aim of our work was estimate the efficiency of different methods of correction of these autoimmune disorders and improving the pregnancy outcome.

Study Methods: 126 diabetic pregnant women with increased serum levels of AT-1 and AT-2 (measured by an original method on a basis of immunofluorescent assay) were divided into 4 groups depending on a kind of received treatment. 42 pregnant women received the heparinum inhalation, 28 – system enzymotherapy (wobenzym), 26 – the specific desensitizing therapy by insulin and 30 – only strictly metabolic control. **Results:** The management of heparinum and wobenzym has resulted in a decrease of the serum contents of AT-1 and AT-2 on 60-65% from initial levels. Usage of insulin as specific desensitizing therapy also has resulted in a decrease of studied antibodies on 62%. In group with only strictly metabolic control the levels of antibodies significantly did not vary. The positive influencing of selected methods of therapy on gestation and neurological status of newborns is marked.

Conclusions: The therapy, lowering specific serum immunoreactivity in diabetic pregnant women, allows to achieve the better outcome of pregnancy for fetus and newborn and to optimize tactics of management.

FC3.17.08

ASSOCIATION BETWEEN GLYCOSYLATED HEMOGLOBIN IN THE FIRST TRIMESTER OF PREGNANCY AND MAJOR FETAL MALFORMATIONS

V. Mazneikova, S. Ivanov, K. Todorova, P. Popivanova
State University Hospital of Obstetrics and Gynaecology "Maichin Dom", Sofia, Bulgaria

Objectives: The aim of the study was to evaluate the incidence of major congenital malformations among unselected pregnant women with insulin-dependent diabetes mellitus and to determine whether a consistent association can be demonstrated, after adjustment for maternal age and White classification, between glycosylated hemoglobin (HbA1c) values in the first trimester of pregnancy and fetal outcome (major malformations).

Study Methods: The retrospective study comprised 180 unselected pregnancies complicated with pre-existent insulin-dependent diabetes mellitus admitted in the High Risk Pregnancy Department between 1995 and 1999. The patients were referred from regional hospitals which did not fulfill the guidelines for the management of pregnancy in diabetic women. Only 2% of pregnancies were planned. All diabetic patients had HbA1c determinations in the first trimester of pregnancy. Women with gestational diabetes were excluded from the study.

Results: Among 180 pregnancies, 121 (68%) resulted in a liveborn infant, 27 (15%) aborted spontaneously, five (2%) resulted in stillbirth, and 27 (15%) were terminated. Of the terminations, twenty were for congenital malformation. The prevalence of congenital malformations varied between 13 and 15% compared with 2% in the general population.

Relative risk calculations indicated a highly significant and consistent correlation between HbA1c values above 7% and major fetal malformations after adjustment for differences in maternal age and White classification.

Conclusions: In an unselected population the infants of women with pre-existent insulin dependent diabetes mellitus have a 6-8-fold greater risk of a congenital malformation than infants in the general population. Our data support a clinically significant and consistent relationship between fetal malformations and HbA1c in the first trimester of pregnancy of mothers with pre-existent insulin-dependent diabetes mellitus.

FC3.17.09

HAVING INSULIN THERAPY IN INADEQUATE GLUCOSE TOLERANCE

S. Djordjevic, M. Gojnic, S. Petkovic, T. Mosic, University of Belgrade, Clinical Centre of Serbia, Institute for Gynecology and Obstetrics, Belgrade, Yugoslavia

Objectives: The aim of this study was to present the necessity of making frequent test of glucosae intolerance in high risk pregnancies.

Study Methods: Last year we started to make routine repetition of oral glucosae tolerance test (OGTT) in pregnancies. We looked after postprandial glucose in all women. We made the diabetic diet and in some cases insulin therapy.

Results: In 81.25% (13 women of the 16 examined) the test was pathological at the end of the second trimester, and in the first one it was normal. In 76.9% of pathology second test, we gave insulin to future mothers and in only 23% diabetic therapy was adequate.

Conclusions: We wanted to suggest that the necessity of routine repeated OGTT, in cases when it was normal in first trimester and a more frequent use of insulin in those cases.

FC3.18 ENDOMETRIAL AND OVARIAN CANCER PROGNOSTIC MARKERS

FC3.18.01

ASSOCIATION OF CYCLIN D1 GENE (CCND1) POLYMORPHISM AND CLINICAL OUTCOME IN EPITHELIAL OVARIAN CANCER
K.K. Dhar, R.E.J. Howells, C.W.E. Redman, P.W. Jones, R.C. Strange, A.A. Fryer, P.R. Hoban, Centre for Cell and Molecular Medicine, University of Keele School of Postgraduate Medicine, North Staffordshire Hospital, Stoke-on-Trent, UK, Department of Obstetrics and Gynaecology, City General, Stoke-on-Trent, UK, Department of Mathematics, Keele University, Staffordshire, UK.

Objectives: The cyclin D1 gene (CCND1) contains a frequent polymorphism (A/G substitution) within the splice donor region of exon 4. CCND1 Genotype is associated with clinical outcome in non-small cell lung cancer and squamous cell cancer of the head and neck. In this study we investigate the influence of CCND1 genotype on clinical outcome in 138 women with epithelial ovarian cancer.

Study Methods: CCND1 genotypes were identified from peripheral blood DNA by polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP) analysis. Patients CCND1 genotypes were compared with clinical details, tumour characteristics, response to chemotherapy, progression free interval and survival data.

Results: The frequency of CCND1 genotypes in the cases and 191 unrelated women controls were similar ($p=0.29$). We observed no correlation between the genotypes and FIGO stage, amount of residual tumour, differentiation and histological type of the tumour and response to chemotherapy. There was no significant difference in overall survival and progression free interval (PFI) among patients with different genotypes. Analysis of data from patients who responded to postoperative chemotherapy revealed that women with CCND1 AA genotype was associated with early disease progression ($p=0.020$, HR 4.58, 95% CI 1.27-16.48) and reduced survival ($p=0.026$, HR 4.48, 95% CI 1.19-16.79) compared to that of CCND1 AG and GG genotypes.

Conclusion: These data show that CCND1 genotype does not influence overall prognosis in epithelial ovarian cancer, however, it is associated with disease progression following initial response to chemotherapy.

FC3.18.02

TYPE III AND TYPE I COLLAGEN METABOLITES AS PREDICTORS OF PROGNOSIS IN OVARIAN CANCER

M. Simojoki*, M. Santala*, J. Risteli**, L. Risteli**, A. Kauppinen*
*Dept. OB/GYN, Oulu University Hospital, 90220 Oulu, FINLAND
**Dept. Clin. Chemistry, Oulu University Hospital, 90220 Oulu, Finland

Objectives: The aim of the study was to investigate the usefulness of aminoterminal propeptide of type III procollagen (PIIINP) and carboxyterminal telopeptide of type I collagen (ICTP) in relation to CA 125 in predicting prognosis of ovarian cancer patients.

Study methods: Fifty-six women with epithelial ovarian cancer were studied through PIIINP, ICTP and CA 125 determinations from serum samples collected before operation and three, six, nine and 12 months

CI 13.6-77.2). In addition, the NPV of normally sited placenta was 99.8% (95% CI 98.7-99.9).

Conclusions: The placental site does not seem to have any influence on the subsequent admission rates for antepartum haemorrhage. A low-lying placenta at 20 weeks scan does not warrant a routine repeat scan in third trimester, but rescanning those with placenta covering os, particularly if posteriorly sited, appears to be more cost effective. Furthermore, an apparently normal placental position at 20 weeks scan is very reassuring indeed, but it still does not absolutely exclude major placenta praevia in later pregnancy.

P3.19.05

COMPARING THE VAGINAL AND RECTAL APPROACH FOR MEASURING THE FEMALE URETHRA WITH THREE-DIMENSIONAL ULTRASOUND

D. Stutterecker, W. Umek, O. Preyer, E. Hanzal, Urogynecology Unit, Department of Gynecology and Obstetrics, University Hospital, Vienna, Austria

Objectives: The aim of this study was to assess differences in urethral measurements by comparing transvaginally and transrectally acquired images of urethral and periurethral tissues.

Study methods: We examined 68 women (mean age 51.3 ± 18.4 years) using a mechanical sector probe (7.5 MHz) with real-time and three-dimensional (3D) facilities on a Combison 530D (Kretztechnik, Austria). The probe was applied both vaginally and transrectally. The stored images allowed detailed morphologic assessment of the urethra including the measurement of volumes in three perpendicular planes. Length of the urethra, length, maximum thickness and volume of the rhabdosphincter, maximum thickness of the inner part of the urethra (consisting of smooth muscle, submucous vascular plexus and urothelium) were measured. SPSS statistical software system was used for calculation.

Results: Both vaginal and rectal scans were tolerated well. Values for length of the urethra (27.8 ± 3.6 mm vaginally vs. 27.7 ± 5.0 rectally), length (16.5 ± 4.3 vs. 15.7 ± 3.3), thickness (6.1 ± 1.4 vs. 6.3 ± 1.8) and volume (0.7 ± 0.3 ml vs. 0.8 ± 0.4) of the rhabdosphincter did not differ between the two methods. The inner layer of the urethra was significantly thicker when examined vaginally (11.5 ± 2.3 vs. 8.8 ± 1.5 ; $p < 0.001$).

Conclusion: Vaginal and rectal approaches of 3D-ultrasound provide equal values for most female urethral structures. However, the part of the urethra consisting of smooth muscle and vascular plexus appears to be compressed on vaginal scans.

P3.19.06

DOPPLER VELOCIMETRY IN THE ADRENAL ARTERY IN THE HUMAN FETUS FOR THE DETECTION OF FETAL STRESS

Y. Fujita, S. Satoh, S. Yanai, K. Tsukimori, H. Nakano, Dept. OB/GYN, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Objectives: The aim of the study is to clarify the age-related chronological changes and hemodynamic aberrations in complicated pregnancies in the velocity of waveforms of the fetal adrenal artery.

Study Methods: A total of 125 cases between 24 and 41 weeks' gestation are included in this study. In these, 108 cases had normal pregnant course with reactive NST, no structural or growth abnormality, and no neonatal asphyxia. Other 17 cases had fetal complications; 4 cases with suspected IUGR, 10 with structural abnormality, 2 with non-reactive NST and 1 with oligoamnios. After detecting the middle adrenal artery by color Doppler flow imaging, velocity waveforms are recorded in condition without fetal movements. The RI value was calculated as the average from 2 consecutive cardiac cycles in each case. Using the data obtained in normal cases, the regression analysis was made for every 2-week interval from 24 to 41 weeks' gestation. The deviation of RI values was investigated as for cases with fetal complications.

Results: In normal cases, RI values in fetal adrenal artery decreased gradually with advancing gestational age. The means values at 24 and 41 weeks are 0.74 and 0.66 respectively ($RI = -0.0006wk^2 + 0.034wk - 0.0259$, $R^2 = 0.964$). In cases with fetal complication, 7 cases had RI values below the mean-2SD. Out of 7, 3 cases (3/7; 42.9%) had fetal hypoxia, fetal anemia and insufficient feto-placental circulation.

Conclusion: In normal pregnancy, it was found that vascular resistance toward fetal adrenal gland gradually decreases with advancing gestational age, reflecting developing vascular network, and that it changes in lower values in fetuses with hypoxia, anemia and insufficient feto-placental circulation, indicating dominant blood flow in the adrenal gland under hypoxic and/or anemic condition.

P3.19.07

DOWN'S SYNDROME RISK ASSESSMENT - COMBINED SECOND TRIMESTER SERUM SCREENING AND ULTRASONOGRAPHY

V. Dumitrova, T. Chernov, V. Mazniskova, I. Kremensky, State University Hospital "Mairich Dom", Sofia, Bulgaria

Objectives: To assess sensitivity and necessity for invasive testing in second trimester Down's syndrome [DS] screening based on serum tests alone and on serum tests combined with genetic sonogram [GS].

Study Methods: Two methods for second trimester DS risk assessment were compared in a group of 1150 patients; 227 (19.7%) of them above the age of 37. Serum screening [SS] with two markers - AFP and free hCG - was going on prospectively. The cut-off risk value for invasive testing was 1:250 at birth. Parallel with that DS risk obtained from the SS was recalculated depending on the results from the GS. In the absence of fetal anomalies or sonographic markers for chromosomal defects risk was reduced by 40%. In the presence of specific ultrasound markers (increased nuchal fold thickness, short femur, echogenic bowel, pyelectasis) risk was corrected by specific factors proposed in literature. Fetal anomalies were considered an indication for amniocentesis despite the results from the SS.

Results: There were 183 abnormal SS test results in the group studied (15.9%) and 11 (0.95%) chromosomally abnormal fetuses (8-DS, 3 - other aneuploidies). Nine of them were in patients older than 37 and 2 - in younger ones. SS alone detected 8 out of the 11 chromosomally abnormal fetuses (sensitivity 72.7%) and 7 of the 8 DS ones (sensitivity 87.5%). If only the results from the SS were considered 3 cases with chromosomal defects would have been missed - one DS fetus, one with trisomy 18 and one with unbalanced translocation. Abnormal sonograms were found in 34 out of 1150 fetuses (2.9%). 19 of them were in the low-risk SS group (1.97%) and 15 were in the high-risk SS group (8.2%). Five of the DS fetuses had one or more sonographic markers but 3 of them had none. The three fetuses with other but DS chromosomal defects had easily detectable sonographic markers. Risk recalculation based on data from the SS and the GS resulted in overall reduction of the number of high-risk results and amniocenteses required by 37 (20%).

Detection rate was 100% for both DS fetuses and the ones with other chromosomal defects with 12.7% invasive testing. In the 3 cases of DS fetuses without sonographic markers SS risk was so high that it warranted amniocentesis even after risk recalculation.

Conclusions: Combined second trimester SS and GS can reduce the number of amniocenteses required because of positive SS results in a predominantly high-risk population. Detection rate for DS is not affected and the detection rate for other chromosomal defects is increased.

P3.19.08

HYDATIC CYST OF THE BREAST

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Objectives: In Tunisia, the hydatid cyst is an endemic disease but the breast localisation is exceptionally reported. In this poster, a new case is described.

Study Methods: Case report and review of the literature.

Results: We collected one case of hydatid cyst of the breast. The woman was 52 years old and lived in a rural area. The systematic examination of the breast founded a 3 cm nodule. The mammography practiced showed a calcified image of 30 mm. The breast ultrasound showed a well-circumscribed formation of 30 mm, having a heterogeneous echotexture with some membranes that evoked a breast hydatid cyst.

In this case, we found another hydatid localisation in the VIIth segment of the liver. The X-ray investigation of the thorax was normal. The treatment was surgical; it consisted in a simple resection of the cyst allowing a recovery without complications. The histological study gave a confirmation of the diagnosis.

4.2. PRENATAL DIAGNOSIS OF β -THALASSEMIA BY THE PCR BASED METHODS

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In the last few years, the mutations causing $\beta\theta$ -thalassemia have been largely elucidated. New procedures to detect $\beta\theta$ -thalassemia mutations have been developed. All of them are based on PCR methodology. Their main advantages are simplicity and rapidity. This provides prenatal diagnosis of these inherited anemias. The prenatal diagnosis of β -thalassemia is not very frequent in Republic of Serbia. In this case, the screening of prospective parents (with a child affected with thalassemia major) is carried out by reverse dot blot (RDB), ARMS (amplification refractory mutation system) and gapPCR analysis. It is confirmed that mother is a carrier of the mutation β^+ IVS.1 - 110 (RDB and ARMS), and father is a carrier of thalassemic hemoglobin variant Hb Lepore. Both mutations are detected after the analysis of DNA of affected child. The analysis of DNA from chorionic villi have shown that the fetus is a heterozygous for Hb Lepore and not a carrier of mother's mutation.

4.3. ULTRASOUND DIAGNOSIS OF FETAL ANOMALIES BETWEEN 8-16 WEEKS OF GESTATION

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Introduction: The majority of congenital anomalies develop before 12 weeks of gestation. At present routine ultrasound detailed evaluation of fetal morphology is performed usually between 18-24w.g. **Aim:** The aim of the study is to assess the effectiveness of ultrasound for detection of fetal anomalies in pregnancies between 8-16w.g. **Materials and Methods:** 651 unselected pregnant women were examined between 8-16w.g. at a tertiary referral center by two experienced sonographers from 1995 till 1999. Transvaginal and/or transabdominal approach with the equipment of ALOKA SSD 1700 and KONTRON HVCD was used. Gestational age was confirmed by measurement of CRL (up to 12w.g.) or BPD and FL (between 13-16w.g.). Complete evaluation of fetal anatomy was carried out. Fetal karyotyping was performed whenever indicated. **Results:** As a whole 12 cases of structural fetal anomalies were detected (1.8%). In 2 of the cases the anomaly was associated with a chromosomal defect. 5 of the cases were diagnosed before 12 w.g. including 2 cases of anencephaly, 1 case of non-immune hydrops fetalis, 1 case of exencephaly and megacystis, and 1 case of TRAP sequence. The rest 7 cases were as follows: 1 case of amniotic band syndrome, 1 case of Saldino-Noonan syndrome, 1 case of hydrocephaly, 1 case of agenisia renum and encephalocele, 1 case of Prune-belly syndrome, 2 cases of nuchal cystic hygroma. 4 genetic amniocenteses were performed detecting 2 chromosomally abnormal fetuses (trisomy 21 and trisomy 18). **Conclusion:** These findings demonstrate the effectiveness of the 8-16w.g. scan in identifying fetal anomalies. Early ultrasound may detect certain fetal anomalies and may be combined with nuchal translucency scanning for screening of chromosomal abnormalities, different genetic syndromes and cardiac defects. Nevertheless, the existence of variable and late on set fetal anomalies necessitate the supplementation of this scan with the conventional 18-24w.g. scan.

Umbilical and uterine artery blood flow in pregnancies complicated with severe preeclampsia

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Objectives. To analyze the umbilical and uterine blood flow in patients with severe preeclampsia and to find out if there is a correlation between the type of umbilical blood flow and perinatal mortality rate as well as the type of uterine blood flow and maternal complications (placental abruption, eclampsia, pulmonary edema, retinal detachment)

Methods. A retrospective study included 49 patients meeting the criteria for severe preeclampsia. All of them were followed up and managed according to the protocol of the Department. Doppler waveforms were obtained from the umbilical (UmbA) and uterine arteries (UA). The equipment used was Aloka SSD 1700 with power and pulsed Doppler. Women were studied from the time of referral until time of delivery. The majority of patients underwent two or more Doppler studies and only the last one made was considered for analysis. The results from the Doppler measurements were not used to influence the clinical management

Results. There were 6 cases with reverse blood flow, 14 cases with 0 flow, 9 cases with increased RI and 20 cases with normal values of RI in the UmbA. The gestational age at delivery was 32.7 ± 3.09 w.g. The mean birthweight was 1291 ± 748 gr. Caesarean section for fetal distress was performed in 47 out of 49 patients. The perinatal mortality rate was 38%. All babies were admitted to NICU. From the 18 perinatal deaths, the blood flow in the UmbA was reverse in 6 cases, 0 in 11 cases and the RI was high in one of the cases.

No maternal deaths occurred. There were 3 cases of placental abruption, one case of eclampsia, 4 cases of pulmonary edema, one HELLP syndrome and one case of retinal detachment. In all cases the pulsatility in both UA was high with bilateral notching

Conclusion. Absent and reverse UmbA diastolic blood flow are both associated with a high rate of perinatal deaths especially in severely growth retarded infants before 28-30 weeks. Bilateral UA notching is a strong predictor of maternal complications in cases of severe preeclampsia

Second trimester genetic sonogram in Down syndrome risk assessment

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Objectives: To evaluate the usefulness of ultrasound in Down syndrome (DS) risk assessment. The suggestion that normal second trimester sonogram reduces the background DS risk while the presence of certain sonographic markers increases it in a specific way was applied [Snijders R.J.M., Sebire N.J., Nicolaides K.H. *Assessment of risks. In: Ultrasound markers to detect chromosomal defects* (1995), Eds.: R. J. M. Snijders, K. H. Nicolaides, The Parthenon Publishing Group]. Design & methods: Second trimester serum screening [SS] and a genetic sonogram [GS] were performed in 495 singleton pregnancies. Patients with DS risk at birth 1:250 or higher were classified as screen-positive. The following abnormal sonographic findings were considered: structural defects, nuchal abnormalities (increased nuchal fold thickness, cystic hygroma), short femur, echogenic bowel, pyelectasis, choroid plexus cysts. Karyotype was obtained after amniocentesis or normalcy was confirmed after delivery. Retrospective recalculation of DS risk for every patient was performed on the basis of the results from the SS and the GS. If none of the listed markers was present DS risk was reduced by 40%. If sonographic markers were detected individual risk was recalculated with the proposed by Snijders and Nicolaides factors. Finally, individual risks were calculated on the basis of one specific risk and data from the GS alone. Percentage of invasive testing required and detection rate were compared for the three approaches for risk assessment. **Results:** 30,4% of the patients were above the age of 35. There were 57 abnormal serum test results (11,5%) and 3 chromosomally abnormal fetuses (0,6%) - two with Down and one with Turner syndrome. If only the results from the SS were considered the fetus with Turner syndrome would have been missed. 20 out of 488 fetuses (4,1%) had abnormal sonograms. 16 of them were in the low-risk group (3,6% from the GS in the group), including the fetus with Turner syndrome and 4 - in the high-risk group (7%), including the two fetuses with Down syndrome. Recalculation of DS risk based on data from the SS and the GS resulted in overall reduction of the number of high-risk results by 14. Thus 8,6% invasive testing would be required and all chromosomally abnormal fetuses would be detected. Finally, risk was recalculated on the basis of maternal age and the results from the GS alone. With this approach 11,3% amniocenteses would be performed and all the chromosomally abnormal fetuses - detected. **Conclusions:** Negative second trimester genetic sonogram may reduce the number of amniocenteses required because of positive SS results without influencing detection rate. Sonographic and serum screening alone yield similar percentage of invasive testing necessary. Detection rate is difficult to interpret because of the small number of fetuses with abnormal karyotype in the present study but it seems to be improved when serum and sonographic studies are combined.

P69

The effect of fetal neck position on fetal nuchal translucency measurement

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The aim of this study was to determine whether the position of the fetal neck has a significant effect on nuchal translucency measurement. **Method:** A prospective cross-sectional study was carried out on 153 women from an unselected population who underwent transabdominal ultrasonography. The nuchal translucency was measured in the mid-sagittal plane, with the fetal neck in the flexed, neutral and extended positions. Measurements were taken to the nearest 0.1 mm. A paired t-test was used to assess differences in the extended and neutral position nuchal translucency (Δ extended NT) and in the flexed and neutral position nuchal translucency (Δ flexed NT). **Results:** The NT was a mean of 0.59 mm greater than the neutral NT (95% CI 0.53 - 0.65, $P < 0.001$). The flexed NT was a mean of 0.40 mm less than the neutral NT (95% CI 0.36 - 0.41, $P < 0.001$). The repeatability coefficient was lower for neutral NT measurement (0.48) and was higher in the other groups (extended = 1.15, flexed = 0.73). **Conclusion:** The effect of the fetal neck position can make a significant difference to nuchal translucency measurement. The repeatability of measurements is more accurate with the fetal neck in the neutral position. These findings have important implications for clinicians using nuchal translucency to screen the general obstetric population.

(FP72)

FETAL BIOMETRY AND DOPPLER INDICES IN POPULATIONS OF DIFFERENT ETHNIC ORIGIN

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Introduction: It is hypothesized that there are (genetic) differences in fetal growth and fetomaternal doppler indices in fetuses of different ethnic origin which may be important in evaluating normal, excessive or insufficient intrauterine growth.

Methods: A paired control study was performed, linking patients from a Flemish population to patients from Turkish origin and controlling for such confounding factors as parity, age and smoking behaviour. Patients were between 17 and 40 weeks, only uncomplicated pregnancies were included. The following measurements were performed: biparietal diameter (outer to inner); head circumference, transverse cerebellar diameter, abdominal circumference, femur length, pulsatility index of the umbilical artery, pulsatility index of the placental and the aoplacental uterine artery.

Results: It was seen that in almost 80% of cases cranial measurements (biparietal diameter, head circumference and transverse cerebellar diameter) was larger in patients from Turkish origin, this difference was less for the abdominal circumference and femur length (60 %). The same was seen for the resistance to flow in the umbilical artery were in 80 % the pulsatility index was lower in the Turkish population, there were no differences for the uterine arteries.

Conclusions: In this preliminary study it is suggested that the already known difference in birth weight between populations of different ethnic origin in our region is based on differences in fetal growth and fetomaternal circulation that start earlier in pregnancy. A larger population based study including longitudinal and transverse evaluation of fetal growth is in progress.

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(FP73)

IDENTIFICATION OF FETAL GROWTH RETARDATION AND OPTIMAL TIMING OF DELIVERY BY THIRD TRIMESTER FETAL BLOOD FLOW EXAMINATIONS

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Introduction: We established the reference ranges for Resistance index (RI) and for Pulsatility Index (PI) between 28th and 42nd week of gestation by serial Doppler examinations of fetal descending aorta, Umbilical Artery, and Middle Cerebral Artery (MCA) in 1000 normal pregnancies

Method: Our purpose was to study the blood flow velocity patterns of 100 infants who were born small for gestational age. We also analysed the results of those 30 cases where increased risk of fetal hypoxia was expected on the basis of the centralised

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fetal circulation indicated by significantly elevated aorta RI and PI with a coexisting drop of the MCA RI and PI. (Elevated Cerebral Index)

Results: The results show that the growth retarded fetuses were characterised by significantly higher RI and PI values in the Aorta and in the Umbilical Artery as well. The parameters of MCA however were found in normal range

Twenty of thirty cases with centralised fetal circulation were also examined by Oxytocin Challenge Test (OCT) that were all positive except one, confirming increased risk of fetal morbidity. All of the 30 pregnancies were terminated. 10 mature, 14 growth retarded and 6 discordant twins were born without perinatal loss. The amniotic fluid was meconium stained in 7 cases.

Conclusion: We concluded that the third trimester fetal blood flow examination combined with fetal ultrasound proved to be useful method in the identification fetal growth retardation and in the assessment of fetal well being. The routine examination of MCA flow pattern recommended in order to detect centralised circulation indicating impending fetal hypoxia. Doppler examination is especially useful for the optimal timing of delivery, where invasive tests (amniocentesis, OCT, cordocentesis) are contraindicated.

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(FP74)

DOPPLER STUDY OF THE UTEROPLACENTAL AND FETOPLACENTAL CIRCULATION IN PREGNANCIES COMPLICATED WITH FETAL ABNORMALITIES

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Introduction: A prospective study of 41 singleton pregnancies complicated with fetal abnormalities was carried out to establish the diagnostic value of uterine and umbilical artery Doppler findings.

Method: The cases were divided in two groups. Group I included 23 major abnormalities. All but three pregnancies were terminated. Group II included 18 compatible with life abnormalities. The pregnancies were followed up till delivery. The uterine and umbilical artery resistance index (RI) and systolic/diastolic ratios (S/D) were measured and compared to the normal ones for the corresponding gestational age.

Results: The uterine arteries' RI and the S/D ratios were normal in all cases. Abnormal umbilical artery Doppler findings were found more frequently in group I compared to group II (60.8% versus 22.2%). Intrauterine growth restriction (IUGR) was found in 24.4% of all fetuses. However, the percentage was higher in group I - 30.4% versus 16.7% in group II. IUGR was accompanied by abnormal umbilical artery Doppler findings only half of the cases. Among the 17 liveborn fetuses from group II there were 11 survivors. Nine of them had normal umbilical artery flow velocity waveforms. Seven of the survivors were born at

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term and 4 - before term. Despite the normal Doppler findings of 88.9% of the fetuses born before term 55.6% of them died at different intervals after delivery.

Conclusion: The results from the study should be discussed with caution since data concerning fetal karyotype are incomplete. Nevertheless it may be concluded that: 1). The uteroplacental circulation is not changed in pregnancies with fetal abnormalities. 2). The fetoplacental circulation changes in a significant number of cases. This is more common when major anomalies are present. 3). IUGR is not always accompanied by changes in the fetoplacental circulation. 4). If the fetus is immature perinatal outcome might be unfavourable despite the normal umbilical artery Doppler findings.

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(FP75)

THE INFLUENCE OF MATERNAL OXYGEN ADMINISTRATION ON FETAL POWER DOPPLER IMAGING AND VELOCIMETRY IN NORMAL AND HIGH-RISK PREGNANCIES

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Introduction: The aim of the study was to evaluate tissue blood flow in the fetal brain, lung and liver before and after maternal oxygen administration in normal and high-risk pregnancies by means of computed Power Doppler (PD) images.

Methods: PD signals were recorded in 18 normal and 22 complicated singleton pregnancies between 31 and 41 weeks of gestation. Preset PD system installations were used during examinations. Images from PD scan were recorded on S-VHS tape and transmitted for computer analysis. Mean PD signal intensity was recorded for fetal brain, lung and liver before and after maternal oxygen administration. The fetal middle cerebral artery (MCA) and main pulmonary artery (PA) flow velocity waveforms were also recorded and analysed for pulsatility index (PI).

Results: A decrease in PD signal values was noticed in fetal brain, liver and lung in normal and in fetal lung high-risk pregnancies. MCA and PA PI increased in both groups studied.

Conclusions: The absence of circulation changes observed in high-risk pregnancy during maternal oxygenation might suggest impaired placental perfusion. Therefore oxygen administration may be of limited value in high-risk pregnancies where needed.

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(FP76)

THE EFFECTS OF PATHOLOGIC UMBILICAL ARTER DOPPLER WAVE FORM STUDIES ON FETAL OUTCOME: THE ABSENCE OF END-DIASTOLIC

FLOW AND THE PRESENCE OF REVERSE BLOOD FLOW

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Introduction: In the presence of reverse blood flow the fetal outcome is worse than in the absence of end-diastolic flow.

Materials and Methods: Perinatal data of 56 cases who delivered between 1994-1997 with absent end-diastolic blood flow or present reverse blood flow during umbilical artery doppler studies was analysed retrospectively. The data was evaluated with the regard to the time interval between pathologic doppler values and the first recognition of the pathologic NST value, 5th min. APGAR score, perinatal mortality, presence of SGA and the time period spent in Neonatal Care Unit.

Results: Out of 56 patients, in 42 the end-diastolic flow was absent and in 14 reverse blood flow was present. No significant differences could be observed between two groups regarding APGAR scores, presence of SGA, time spent in NICU and perinatal mortality. When the groups were subdivided according to the presence of oligohydramnios and compared according to the fetal outcome no significant differences could be found.

Conclusion: The pathologic findings in umbilical artery doppler studies indicates worse perinatal outcome but there is no significant difference between absent end diastolic blood flow and reverse blood flow.

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(FP77)

IS THE PLACENTAL SLUICE FLOW PHENOMENON RECIPROCAL?

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Introduction: Intraplacental shifts between maternal and fetal blood volumes may be the basic event for the sluice flow phenomenon. This phenomenon is believed to be reciprocal. This study tested the hypothesis that fetoplacental volume expansion affects intervillous flow and hence interplacental vascular resistance.

Methods: Eleven women with anemic fetuses had intrauterine fetal blood transfusion at 22-35 weeks. The fetoplacental intravascular volume was expanded by an estimate of 17-71%. The umbilical and intraplacental interplacental vascular resistance was measured immediately before and after the procedure by Doppler velocimetry. Simple linear regression analysis and one-tailed paired t-test were used for statistical evaluation, with a P-value < 0.05 considered significant.

Results: Hemoglobin concentrations increased by 24-86 g/L, but no flow variable was significantly changed after the transfusion. This was valid also when only cases with a volume expansion of >30% (n = 15) were compared. A positive correlation was found

VI. 85, 86

7.3. THERAPEUTIC EFFECT OF ZINC ON LIPIDIC AND CARBOHYDRATE METABOLISM IN DIABETIC RATS

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The research programme was carried out using white, male, Wistar rats, distributed in 4 groups: M- control, Allx- rats which received alloxan, Zn- rats which received zinc and Allx + Zn- rats which received both alloxan and zinc. Diabetes was induced by injecting a unique dose of alloxan, i.v., and the zinc was administered by gavage (daily).

After 6 weeks blood was drawn from the retroocular sinus in order to assess the values of glucose, the lipoprofile, and the MDA activity.

The results of the experiment showed the benefic influence of the zinc as follows: the reduction of hyperglycemia and the absence of glucosuria in diabetic rats, a drop in the level of serum cholesterol and triglycerides and especially an increase of the amount of Col-HDL; the limitation of the lipoperoxiding process, as indicated by the reduction of MDA.

That proves an increase of existing insulin activity and an insulin-like effect of Zn. Diabetes evolution, especially in young people could be much better by adding certain Zn soluble salts to the basic treatment.

Further research activities are meant to establish whether the role of zinc was overestimated or misunderstood.

7.4. DO HIGH VALUES OF AMNIOTIC FLUID INSULIN PREDICT FETAL MACROSOMIA IN GESTATIONAL DIABETIC PREGNANCIES?

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Fetal macrosomia continues to complicate the pregnancies in diabetic women. These babies are prone to increased mortality and morbidity. There is a good fetal outcome in women with gestational diabetes with selective insulin therapy based on maternal glycaemic levels. Nevertheless, it is accepted that the most sensitive, practical form of selection for intensive insulin therapy is the detection of fetal hyperinsulinaemia by measurement of amniotic fluid insulin on amniocentesis specimens.

14 pregnant women were included in a pilot study. The patients had been screened at 28 weeks' gestation after a 75g glucose load. Amniocentesis was performed in the 28th gestational week and the values of immunoreactive insulin (IRI) were determined using RIA. Values of IRI > 12.8 mU/ml were considered pathologic. Insulin treatment was initiated if plasma glucose level > 11.2 mmol/l at 2 hour after 75g loading or after treatment with diet the patient still had preprandial glucose levels persistently > 6.5 mmol/l. Macrosomia was defined as a birthweight > 4000 gms. In 5 of the cases the values of the amniotic fluid IRI were pathologic. 3 macrosomic fetuses were delivered to mothers treated by a diet alone. Two babies were under 4000 gms. In one of the cases the pregnant woman received insulin treatment and in the other the patient was on a diet alone. In 9 of the cases the IRI values were in the normal range and none of the fetuses were macrosomic at delivery.

Despite the small number of cases we conclude that maternal parameters can not be used to predict or exclude fetal diabetogenic hazards. Macrosomia is associated with elevated amniotic fluid insulin. We advocate insulin treatment in cases of elevated amniotic fluid insulin.

7.5. DOPPLER STUDY OF THE BLOOD FLOW IN THE UMBILICAL ARTERY IN THIRD TRIMESTER DIABETIC PREGNANCIES

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121 pregnancies complicated by diabetes mellitus were included in a prospective study. The

purpose was to investigate the relation between glycaemic control and flow velocity waveform (FVW) and the predictive value of umbilical artery (u.a.) FVWs for antenatal fetal compromise. U.a. resistance index (RI) was measured from 30 weeks. Glycaemic control was unrelated to u.a.FVW values. Abnormal u.a.RI was found in 3 pregnancies. In 5 pregnancies there was evidence of fetal compromise but only 2 of these pregnancies had abnormal FVW values.

Long-term glycaemic control does not seem to affect u.a.RI. Abnormal u.a.RI is a significant predictor of fetal compromise in diabetic pregnancy, but fetal compromise can occur in association with normal RI values.

7.6. TYROSINE AND TRYPTOPHAN AND THEIR METABOLITES IN THE DIABETIC PATIENTS

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Diabetic neuropathy is a common complication of diabetes. It was reported that in diabetic patients with neuropathy plasma noradrenaline concentration is low, while there are some reports that the noradrenaline contents in plasma were not different between the diabetic patients and the control. We analysed the contents of tyrosine, tryptophan and their metabolites in the plasma of diabetic patients, and the results were compared to those of the normal. Substances were analysed by the 3-dimensional HPLC-system: Neurochem (ESA Inc, Bedford, MA, USA). The plasma levels of tyrosine, noradrenaline, tyramine, VAM, VA, dopac, tryptophan, serotonin and melatonin were not different between the diabetic patients and the normal, but that of kynurenine increased in the diabetic patients. It is known that quinolic acid, a metabolite of kynurenine stimulates NMDA receptor and may produce neuropathy. Thus, it is suggested that the increased plasma level of kynurenine in the diabetic patients is a relation to neuropathy.

7.7. DEFENCES AGAINST FREE RADICALS IN MUSCLE

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The occurrence of oxygen free radicals is an attribute of normal aerobic life. 3-5% of total oxygen used in aerobic metabolism is resulted with reactive oxygen metabolites. Physical exercise is associated with a 10-15 fold increase in oxygen consumption. A large number of recent studies have indicated that physical exercise induces oxidative stress; a state where the pro-oxidant forces overwhelm the antioxidant defence capacity of the body. Oxidative stress has been hypothesized to remarkably contribute to skeletal muscle fatigue and muscle damage.

A variety of endo- and exo-genous antioxidants act in concert to protect against oxidative stress. Glutathione (GSH) plays a central role in the synergism. Apart from enzymatic and non-enzymatic decomposition of reactive oxygen species (ROS), reduced glutathione (GSH) is suggested to be implicated in maintaining a favourable redox milieu of crucial antioxidants, vitamins E and C. Our studies have shown that GSH dependent antioxidant protection is considerably affected by the state of physical activity; both sprint and endurance type training regimes enhances and chronic inactivity diminishes such protection. Our experiments with cultured muscle cells (L6 myoblasts) show that muscle cells are active in GSH synthesis with a ≈ 3 mM intracellular concentration and a rapid turnover. Exercise associated increase in plasma levels of oxidized glutathione (GSSG) is perhaps mainly contributed by GSSG expelled from the active skeletal muscle.

Recently, we investigated the association between exercise intensity and related oxidative stress in nine healthy young men who exercised for 30 mins at their aerobic (AcT) and anaerobic (AnaCT) thresholds. A single bout of exercise, as carried out during the Max, AcT and AnaCT tests, induced blood GSH oxidation. Compared to that following AcT, exercising at the AnaCT was associated with a marginally higher extent of oxidative stress.

12.7 Pitfalls in prenatal USD of fetal skeletal dysplasias

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The majority of skeletal dysplasias/SD/ with neonatal manifestations are lethal and affected families may greatly benefit from prenatal diagnosis and discussion of possible options/termination, method of delivery, neonatal resuscitation/ if an abnormal fetus is detected. In cases of positive family history the PND is relatively easier, compared to sporadic occurrence of the disease. As a rule, the experienced ultrasonographer could make the diagnosis of a SD, but some mistakes are possible in the correct identification of the disorder.

Authors present their experience in USPND of 10 cases with SD, emphasising the importance of markers that must be carefully looked for, especially hypomineralisation of skull and bone fractures in Q1, 4, disproportion between BPD and FL in achondroplasia, tibial length and shape in short rib-polydactyly syndrome type II.

One of the main conclusions is the necessity of close collaboration between the ultrasonographer and an experienced clinical geneticist in the follow-up of pregnancies at high risk of fetal SD.

12.8 Spontaneous mitotic activity of peripheral blood cells in system in vitro in pregnancy

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The preliminary results of our study on 12 pregnant women show a presence of a high rate of spontaneous mitotic activity of peripheral blood cells in system in vitro. We did not add any of stimulation factors that enter cells in culture into mitosis.

Cytogenetic analyses show a possibility of the complete karyotype analysis of these cells in 10 patients. In 9 patients we found out normal female karyotype (46,XX) and a normal male karyotype (46,XY) in 1 patient. PCR reaction, with primers which amplify whole open reading frame of testis determining gene SRY, are in high correlation with cytogenetic analyses and with the sex of newborn children. This gene could be presented in maternal circulation only if she carry a male fetus.

More investigation is needed to prove the origin of these cells, maternal or fetal. The sense of their intensive spontaneous mitotic activity is a question to be discussed.

0.3 Registration of congenital anomalies and prenatal US diagnosis

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Regional Registry of congenital anomalies (CA) in Sofia collected 150 new families in 1996, registered because of terminated pregnancy/14/, stillborn/12/ or liveborn/124/ baby with CA, amongst a total number of 10229 followed pregnancies/1.47%. From genetic point of view the registered anomalies could be subdivided into chromosomal abnormalities-16(10.7%), single gene defects-16(10.7%), multifactorial anomalies-80(53.3%), environmental-4(2.7%) and of unknown etiology -34(22.7%). US prenatal diagnosis has been performed in 81% of pregnancies with conceptuses affected of CA. Isolated or multiple CA had been detected before birth or termination in only 22.4% of tested pregnancies. The detectability of different types of CA before birth varies considerably: 6.7% in chromosomal disorders, 14.3% in monogenic defects, 22.2% in multifactorial anomalies, 75% in environmental disorders.

In conclusion, prenatal US diagnosis as it is practiced at the moment shows low efficiency, especially regarding the early diagnosis of chromosomal abnormalities and congenital heart disease. A critical approach in respect to the qualification of specialists and organisation of US screening of pregnant women seems to be quite necessary.

0.4 Education and certification of genetic counselors

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Genetic counseling is defined by the American Society of Human Genetics as a communication process which deals with the human problems associated with the occurrence, or risk of occurrence, of a genetic disorder in a family. The first graduate program (Master's degree) in genetic counseling started in 1969 at Sarah Lawrence College, NY, USA, while in 1979 the National Society of Genetic Counseling (NSGC) was established. Today, there are 29 programs in U.S.A. offering a Master's degree in Genetic Counseling, five programs in Canada, one in Mexico, one in England and one in S. Africa. Most of these graduate programs offer two year training, consisting of graduate courses, seminars, research and practical training. Emphasis is given in human physiology, biochemistry, clinical genetics, cytogenetics, molecular and biochemical genetics, population genetics and statistics, prenatal diagnosis, teratology and genetic counseling in relation to psychosocial and ethical issues. Certification for eligible candidates is available through the American Board of Medical Genetics (ABMG). Requirements for certification include a master's degree in human genetics, training at sites accredited by the ABMG, documentation of genetic counseling experience, evidence of continuing education and successful completion of a comprehensive ABMG certification examination. As professionals, genetic counselors should maintain expertise, should insure mechanisms for professional advancement and should always maintain the ability to approach their patients.

REGISTRATION OF CONGENITAL ANOMALIES AND FETAL DYSMORPHOLOGY

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Registration of congenital anomalies (CA) according to EUROCAT criteria and requirements was undertaken in the city of Sofia from the beginning of 1996. The method allows prenatal detection and follow up of fetuses with isolated and multiple congenital anomalies. Over a period of 6 months 5196 pregnancies came to birth or were terminated for various reasons. 73 families (1.4%) have been registered because of CA in a terminated fetus, newborn baby or an infant under 1 year of age. This report summarizes the results of US testing follow-up and management of 23 pregnancies with increased genetic/environmental risk (9.2) or fetal structural anomalies, detected by ultrasound (12). In the latter group 1 false positive result has been proved and 11 fetuses showed isolated or multiple CA as follows: chromosomal - 3 (45, XO, trisomy 13, trisomy 18), single gene defects - 3 (Meckel syndrome, polycystic kidney disease, chondrodysplasia punctata), other MCA syndromes - 3 (acardic monozygotic twin monster syndrome, Cantrell syndrome, abdominal wall defect), (11), isolated major congenital anomalies - 2 (ventriculomegaly). The registration of CA during pregnancy is a powerful method for studying the normal variation of different fetal structures, diagnosis and improvement the medical care of preexisting diseases states in the families, as well as early diagnosis of an increasing number of nonchromosomal, nonmetabolic dysmorphic syndromes. At the time being sensitivity and specificity of the prenatal US testing remains relatively low that needs further debate concerning acceptability and criteria for efficiency of the mass US screening of pregnant women.

FIRST TRIMESTER DIAGNOSIS OF FETAL ABNORMALITIES BY TRANSVAGINAL SONOGRAPHY

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A prospective sonographic study of fetal anatomy was carried out in 125 pregnancies between 9 and 14 weeks of gestation using both transabdominal and transvaginal scanning. The study included 50 high risk patients and 75 low risk ones. In 3 cases (2.4%) major fetal anomalies that were missed at transabdominal scanning were diagnosed by transvaginal examination. They included: a case of anencephaly, a case of exencephaly and megacystis and a case of monoamniotic twin pregnancy with twin reverse arterial perfusion sequence. In the first two cases pregnancy was terminated by the end of the first trimester. In the third one intrauterine death in the 14th week of gestation occurred.

The study confirms the superiority of transvaginal ultrasound examination in the first trimester of pregnancy, minimizing some of the technical difficulties of transabdominal scanning, early diagnosis of fetal anomalies and termination of pregnancy by D&C possibilities for rapid karyotyping if necessary. However, high qualification and experience of the examination are required. Some critical aspects of the early diagnosis of fetal anomalies (possible diagnostic errors, absence of histopathologic confirmation in most of the cases) must be considered too.

REGISTRATION OF CONGENITAL ANOMALIES AND FETAL DYSMORPHOLOGY

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Registration of congenital anomalies /CA/ according to EUROCAT criteria and requirements was undertaken in the city of Sofia from the beginning of 1996. The method allows prenatal detection and follow up of fetuses with isolated and multiple congenital anomalies. Over a period of 6 months 5251 pregnancies came to birth or were terminated for various reasons. 69 families /1.3%/ have been registered because of CA in a terminated fetus, newborn baby or infant under 1 year of age.

This report summarizes the results of US testing, follow up and management of 23 pregnancies with increased genetic/environmental risk (9/2) or fetal structural anomalies, detected by ultrasound /12/. In the latter group 1 false positive result has been proved and 11 fetuses showed isolated or multiple CA as follows: chromosomal - 3/45,XO, trisomy 13, trisomy 18/, single gene defects - 3/Meckel syndrome, polycystic renal disease, chondrodysplasia punctata, other MCA syndromes - 3/acardiac monozygotic twin monster syndrome, Cantrell syndrome, abdominal wall defect/CHD, isolated major congenital anomalies - 2/ventriculomegaly/

The registration of CA during pregnancy is a powerful method for studying the normal variation of different fetal structures, diagnosis and improvement the medical care of preexisting pathologic states in the families, as well as early diagnosis of increasing number of nonchromosomal, nonmetabolic dysmorphic syndromes. At the time being the sensitivity and specificity of the prenatal US testing remains relatively low that needs further debate concerning acceptability and criteria for efficiency of the mass US screening of pregnant women

CORDOCENTESIS IN PRENATAL DIAGNOSIS OF GENETIC DISORDERS

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A retrospective study of the cordocenteses performed for a three year period (1993 - 1996) in the University Maternity Hospital at the Medical Faculty in Sofia was made. A total number of 45 procedures were performed by 4 operators. The indications included: advanced maternal age - 9 (20%); previous affected child (either with Down's syndrome or multiple anomalies) - 2 (4.4%); equivocal results from genetic amniocentesis - 5 (11.1%); a parent - carrier of a balanced chromosome translocation - 2 (4.4%); sonographic evidence for isolated or multiple fetal anomalies - 25 (55.5%); IUGR - 2 (4.4%).

In 8 cases (17.7%) the procedure was not successful because of contamination with amniotic fluid or maternal blood. Most frequently the reasons were posterior lying placenta combined with maternal obesity and severe hydramnios or oligohydramnios. No obstetric or neonatal complications after cordocentesis were registered.

In 5 cases (11.1%) the fetal karyotype was abnormal. The following abnormalities were included: 47 XXX (cordocentesis because of maternal age and mosaicism from the amniocentesis), trisomy 18 (sonographically detected diaphragmatic hernia), unbalanced chromosome translocation 45XX trans (13/14) in a case of a parent - carrier of the same defect, 46 XX (del3p) in a case of multiple fetal anomalies and 46 XY (10 q+) - in a case with neonatal death of two children with multiple anomalies.

Despite the comparatively low number of cases it may be concluded that cordocentesis is a valuable procedure for rapid and safe fetal karyotyping after the 20th week of gestation. This is extremely important in the cases of late referral for genetic counselling, failed chorionic villus sampling or equivocal results from second trimester amniocentesis. The incidence of cases with abnormal fetal karyotype in the group studied is very high - 11.1%. Fetuses with sonographically detected anomalies are carriers of chromosomal defects in 8% thus making this group a serious candidate for further invasive prenatal testing.

DIMITROVA Violeta
V. Mazneikova

**FIRST TRIMESTER DIAGNOSIS OF FETAL
ANOMALIES BY TRANSVAGINAL SONOGRAPHY:
A REPORT OF THREE CASES**

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A group of 75 patients with an increased risk of having a child with congenital anomaly were examined by transabdominal and transvaginal sonography between 9 and 12 weeks of gestation (w.g.). Three cases with major abnormalities were diagnosed: 1) Anencephaly. It was strongly suspected in the 9 w.g., documented and confirmed 2 weeks later. Pregnancy was terminated. 2) Exencephaly and megacystis. The diagnosis was established in the 12 w.g. Pregnancy was terminated. 3) Monoamniotic twin pregnancy with acardia and other fetal anomalies (TRAP sequence), diagnosed in the 10 w.g. Pregnancy ended with intrauterine fetal death in the 14 w.g.

In all the cases the diagnosis was confirmed only after transvaginal sonographic examination. The transabdominal examination preceding the transvaginal one could not reveal the true nature of the defects. In the first case incorrect dates were suspected, in the second only megacystis was diagnosed and in the third one the transabdominal sonographic finding could not be interpreted definitely.

The data indicate that transvaginal sonography is an unsurpassed method for very early diagnosis of fetal anomalies. However, some important considerations exist: possible diagnostic errors, patients' objection to very early termination of pregnancy, difficult or impossible pathologic confirmation of the sonographic findings when pregnancy is terminated by D&C.

THE PRENATAL
ULTRASONOGRAPHIC
DIAGNOSIS OF SACROCOCCYGEAL
TERATOMA

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Key words: ultrasound, prenatal diagnosis, sacrococcygeal teratoma

Sacrococcygeal teratoma is a rare, serious malformation, which occurs in approximately 1 in every 40,000 births. Although this condition is well described in the pediatric literature, to our knowledge there have been a few cases in which this condition was diagnosed with prenatal ultrasonography. The anomaly is not uniformly fatal in the neonate but depends on the histologic type and the size of the tumor. Despite of this, the obstetric management is aggressive because of the old concept that a malformed fetus never survives. On the other hand the affected family cannot resist the emotional burden and decides to terminate the pregnancy.

We review the literature and present three cases of antenatally diagnosed sacrococcygeal teratoma.

In the first case the diagnosis was made immediately prior to the vaginal delivery of the infant who died, and the prenatal diagnosis did not influence management.

In the second case the diagnosis was made in the 32nd w.g. in a patient, admitted for threatened premature delivery. Despite the tocolytic therapy labour progressed and in its course during a vaginal examination, the "mass" was deliberately enucleated. The fetus was born dead by exsanguination.

In the third case the anomaly was diagnosed in the second trimester in time for through counseling of the parents. In this case, despite the normal karyotype, the family decided to terminate the pregnancy. We discuss the obstetrics management in each case and point out on what it should be based.