The 8th European Symposium “Prevention of Congenital Anomalies”
Poznań, June 9-10, 2005

Programme:

June, 9th (Thursday)
19.00 Welcome reception (“Młyńskie Koło” Restaurant)

June, 10th (Friday)
8.30 – 18.00 The 8th European Symposium “Prevention of Congenital Anomalies”
8.30-8.50 Welcome ceremony

Session 1 8.50-9.55
Epidemiology of congenital malformations (1)
Chairmen:

8.50-8.55 Invited speaker: Helen Dolk
(S 01) FETAL EXPOSURE TO ENVIRONMENT POLLUTION: THE ROLE OF SURVEILLANCE
EUROCAT Central Registry, University of Ulster, UK

9.10-9.55 Oral presentations:

9.10-9.15 (S 02) A Wiesel1, A Queisser-Luft1, G Stolz1, K Schlaefer2, B Zabel3, M Blettner4, J Wahrendorf5
REPORT ON A CLUSTER OF TRISOMY 21 CASES IN THE REGION OF RHEINHESSEN, GERMANY, IN 2004
1Birth Registry Mainz Model, Joh. Gut.-Univ. Mainz; 2Environmental Epidemiology, DKFZ, Heidelberg; 3Human
Genetics, Children’s Hospital, Joh. Gut.-Univ. Mainz; 4IMBEI, Joh. Gut.-Univ. Mainz; Germany

9.25-9.40 (S 03) MR Krawczyński1 and PRCM Working Group: A Materna-Kiryluk1, J Mejnartowicz1, A Balcar-Boroń2, M
Czerwionka-Szafarska3, E Gajewska4, M Krawczyński5, J Limon6, J Stańczyk7, E Szałwikiewicz-Warowicka8, M
Walczak9, A Latos-Bielinska1
CONGENITAL MALFORMATIONS OF THE ORGAN OF VISION: EPIDEMIOLOGICAL DATA BASED ON
POLISH REGISTRY OF CONGENITAL MALFORMATIONS 1997-2001, DIAGNOSTIC RECOMMENDATIONS
AND GENETIC COUNSELLING.
1Chair and Department of Medical Genetics, University of Medical Sciences in Poznań; 2Department of Paediatrics,
Haematology and Oncology, Medical University of Bydgoszcz; 3Chair and Department of Pediatric Allergology and
Gastroenterology, Collegium Medicum Bydgoszcz, University in Toruń; 4Department of Neonatology, Medical
University in Wrocław; 5Chair and Department of Biochemistry and Bioinformatics, Medical University of Gdańsk;
6Chair and Department of Biology and Genetics, Medical University of Gdańsk; 7Institute of Paediatrics, Maria
Konopnicka Memorial Teaching Hospital No 4 in Łódź; 8Regional Children’s Hospital, Olsztyn; 9II Department of
Paediatrics, Pomeranian Medical University, Szczecin; Poland.

9.40-9.55
(S 04) A Kot, W Błaż, E Pszeniczna, J Rusin
THE ANALYSIS OF FACTORS INFLUENCING HIGH DETECTION RATE OF CONGENITAL HEART
DEFECTS IN THE PODKARPACKIE PROVINCE.
Department of Pediatrics, Regional Hospital in Przeworsk, Poland
Session 2  10.00-10.50
Epidemiology of congenital malformations (2)
Chairmen:

10.00-10.20  Invited speaker: Fabrizio Bianchi
(S 05) THE POTENTIAL OF EUROCAT FOR EPIDEMIOLOGICAL RESEARCH
Unit of Epidemiology, CNR Institute of Clinical Physiology, Pisa, Italy

10.20-10.50 Oral presentations:
10.20-10.35
(S 06) JA Greenacre, FD Tucker, CP Humphreys
GASTROSCHISIS IN WALES - CONTRIBUTION OF THE WELSH CONGENITAL ANOMALY REGISTER
(CARIS)
The National Public Health Service for Wales, The National Health Service and the Congenital Anomaly Register for Wales, UK.

10.35-10.50
(S 07) M Loane, H Dolk, I Bradbury + A EUROCAT Working Group.
INCREASING PREVALENCE OF GASTROSCHISIS IN EUROPE: A YOUNGER MOTHER PHENOMENON?
EUROCAT Central Registry, University of Ulster, UK

10.50-11.10   Coffee break

Session 3  11.10-12.55
Etiology of congenital malformations (1)
Chairmen:

11.10-11.40  Invited speaker: Hans-Hilger Ropers
(S 08) LARGE-SCALE ELUCIDATION OF GENETIC DISEASE AND IMPLICATIONS FOR HEALTH CARE
Max Planck Institute of Molecular Genetics, Berlin, Germany

11.40-12.55 Oral presentations:
11.40-11.55
(S 09) E Bocian¹, B Nowakowska¹, K Borg¹, E Obersztyn¹, I Chudoba², E Kosty³, A Krucek³, J Pietrzyk³, T Mazurczak³
IDENTIFICATION OF ADDITIONAL CHROMOSOMAL MATERIAL WITH CGH AND FISH TECHNIQUES IN PATIENTS WITH PHENOTYPIC ABNORMALITIES
¹Department of Medical Genetics, Institute of Mother and Child, Warsaw, ²MetaSystems GmbH, Altlussheim, Germany, ³Department of Medical Genetics, Polish-American Children’s Hospital, Jagiellonian University, Cracow, Poland

11.55-12.10
(S 10) I Barisic, L Morozin-Pohovski, I Petkovic
MAJOR CONGENITAL MALFORMATIONS AND 22q11.2 MICRODELETION
Children’s University Hospital Zagreb, Croatia

12.10-12.25
(S 11) A Mostowska¹, B Biedziak², P Wójcicki³, K Kobus³, WH Trzeciak¹
MOLECULAR BASIS OF TOOTH AGENESIS AND OROFACIAL CLEFTS IN THE POLISH POPULATION
¹Department of Biochemistry and Molecular Biology, Poznan University of Medical Sciences, Poznan, ²Department of Orthodontics, Poznan University of Medical Sciences, Poznan, ³Department of Plastic Surgery, University of Medical Sciences, Wroclaw, Poland

12.25-12.40
MOLECULAR PATHOGENESIS OF HIRSCHSPRUNG DISEASE – THE SIGNIFICANCE OF POLYMORPHISMS OF RET GENE
Medical University Wroclaw, Poland

12.40-12.55
(S 13) E Pastuła-Mańko, M Piotrowicz, E Kasprzak, E Czichos, J Gadzinowski
Department of Neonatology ICZMP (Polish Mother’s Memorial Hospital Research Institute), Lodz, Poland

13.00-14.30 Lunch and Poster Session
Chairmen of the Poster Session:

Session 4 14.30-15.30
Etiology of congenital malformations (2)
Chairmen:

14.30-15.30 Oral presentations:

14.30-14.45
(S 14) O Lynchak, S Kartashova, V Yelagin, E Omelchenko, N Brezystka, O Tymchenko
CONGENITAL MALFORMATIONS – RISK FACTORS
Institute of Hygiene and Medical Ecology, Ukraine

14.45-15.00
(S 15) MK Bakker¹, WM Meijer², HEK de Walle¹
BIRTH DEFECT AND DRUG EXPOSURE SURVEILLANCE IN THE NORTHERN NETHERLANDS.
¹EUROCAT Northern Netherlands, Department of Medical Genetics, University Medical Centre Groningen.
²Department of Social Pharmacy, Pharmacoepidemiology and Pharmacotherapy, University Institute for Drug Exploration (GUIDE), Groningen, The Netherlands

15.00-15.15
(S 16) ES Draper, J Rankin, A Tonks, KR Abrams, P Burton, JJ Kurinczuk
RECREATIONAL DRUG USE: A MAJOR RISK FACTOR FOR GASTROSCHISIS?
Universities of Leicester, Newcastle, Oxford & West Midlands Perinatal Institute, UK

15.15-15.30
MATERNAL OBESITY AND CONGENITAL ANOMALIES: TEMPORAL CHANGE IN BMI IN EMILIA ROMAGNA, ITALY.
IMER Registry, Medical Genetics Section, University of Ferrara, Italy

15.30-15.50 Coffee break

Session 5 15.50-17.40
Prevention of congenital malformations and prenatal diagnostics
Chairmen:

15.50-16.10 Invited speaker: Lenore Abramsky
(S 18) PREVENTION OF CONGENITAL ANOMALIES BY FOLIC ACID SUPPLEMENTATION
Congenital Malformations Register, Northwich Park Hospital, Harrow, UK
16.10-17.40 Oral presentations:

16.10-16.25
(S 19) E Mierzejewska, ZJ Brzeziński
THE NATIONAL PRIMARY PREVENTION PROGRAM OF NEURAL TUBE DEFECTS IN POLAND
Institute of Mother and Child, Warsaw, Poland

16.25-16.40
(S 20) MI Van Allen, P Stathers, E Cairns, E Boyle, SH Uh, P De Wals
PREVENTION OF NTDs WITH FOLIC ACID SUPPLEMENTATION AND FOOD FORTIFICATION IN BRITISH COLUMBIA, CANADA: OVER A 10 YEAR EXPERIENCE IN A ‘LOW INCIDENCE AREA’
University of British Columbia, Department of Medical Genetics, BC Health Status Registry, and Laval University, Canada

16.40-16.55
(S 21) PA Boyd, E Garne, C DeVigan
EUROCAT SURVEY OF POLICIES FOR PRENATAL SCREENING FOR FETAL ANOMALY OPERATING IN EUROPEAN COUNTRIES
Prenatal Diagnosis Unit, Women’s Center, Oxford radcliffe NHS Trust, Headington, UK

16.55-17.10
(S 22) J Stańczyk, K Niewiadomska-Jarosik, D Tomecka, B Kierzkowska
CARDIOLOGICAL PRENATAL DIAGNOSTICS: A FIFTEEN-YEAR EXPERIENCE
Department of Paediatric Cardiology, Medical University of Łódź, Poland

17.10-17.25
(S 23) P Sieroszewski, E Baś-Budecka, M Perenc, J Suzin
ULTRASOUND DIAGNOSTIC SCHEMA FOR DETERMINATION OF INCREASED RISK FOR CHROMOSOMAL ANEUPLOIDIES IN FOETUS IN THE FIRST HALF OF PREGNANCY
1st Division of Obstetrics and Gynecology, Medical University of Łódź, Poland

17.25-17.40
(S 24) W Wertelecki, T Vihovska, L Yevtushok
IMPACT OF RESOURCE CENTERS ON PARENTAL SUPPORT GROUPS CREATION AND DEVELOPMENT IN UKRAINE
Ukrainian-American Birth Defects Program, Ukraine

17.40-18.00 Closing of Symposium
ABSTRACTS:

Oral presentations:

Epidemiology:

(S 01)
H Dolk
FETAL EXPOSURE TO ENVIRONMENT POLLUTION: THE ROLE OF SURVEILLANCE
EUROCAT Central Registry, University of Ulster, UK
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(S 02)
A Wiesel, A Queisser-Luft, G Stolz, K Schlaefer, B Zabel, M Blettner, J Wahrendorf
REPORT ON A CLUSTER OF TRISOMY 21 CASES IN THE REGION OF RHEINHESSEN, GERMANY. IN 2004
Birth Registry Mainz Model, Joh. Gut.-Univ. Mainz; Environmental Epidemiology, DKFZ, Heidelberg; Human Genetics, Children’s Hospital, Joh. Gut.-Univ. Mainz; IMBEI, Joh. Gut.-Univ. Mainz; Germany
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Introduction: At a prevalence rate of approximately 1:500, trisomy 21 (Tri21) is the most important genetic cause of mental retardation. Environmental factors may play a role and exert a deleterious effect during meiosis II, a sensitive period shortly after conception.

Subjects and methods: The population-based Birth Registry Mainz Model actively surveys Rheinhessen, a region of approximately 400,000 inhabitants. Since 1990, a total of 48,303 newborns have been screened, covering about 90% of all birth in this area. Statistical analysis was performed with 2x2 tables assuming a Poisson distribution.

Results: Between January and June 2004, 8 live births with Tri21 were observed, which exceeds the expected number of about 3-4 live births within a 6-month period. Based on the calculated time of conception of all Tri21 children we found that eleven out of eighteen infants within 2003 were conceived within a period of three months (June to August 2003). From April 1989 until today, a total of 102 newborns and foetuses with Tri21 were recorded, resulting in a ratio of 1:474. A total of 18 cases were documented to be conceived in 2003 (estimated ratio 1:173). The prevalence ratio (RR) for the two periods (1989-2002 vs 2003) is 3.1 (1.9-5.2, p<0.0001). Assuming a Poisson distribution of \( \lambda = 0.6 \), the statistical probability (p) for the occurrence of eleven cases in three months is less than 0.0001.

Discussion: The only proven risk factor for an infant with Tri21 is high maternal age (>35 years). In 2003 33% of mothers of children with Tri21 were older than 34 years compared to 40% in the preceding years. Smoking, maternal irradiation, alcohol consumption, oral contraceptive, and fertility drug use, as further discussed risk factors were statistical similar distributed between Tri21 cases and the rest of the cohort. Hypotheses include the extreme temperatures (>40°C) between June and August 2003, with very low Rhine and ground-water levels. Planned molecular studies will focus on the origin of the extra chromosome 21 to determine the timing of the non-disjunction event (meiosis I vs II). Case-control studies will evaluate environmental factors (incl. climatic stress).

(S 03)
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Introduction. Congenital malformations of the organ of vision increasingly contribute to the causes of severe visual handicap in developed countries. In Poland there have been no population-based studies on prevalence of congenital eye malformations. There are no diagnostic recommendations which refer to the early diagnostics of congenital eye malformations (which is an opportunity for early prevention and treatment, and is the only chance to avoid blindness). Also, there have been no compiled regulations of genetic counselling for this specific group of patients. In this context, the basic assumption of this study was to fill this gap with possibly most complete epidemiological and clinical data with regard to specificity of the diagnostic process and counselling.

The aims of the study were (1) the assessment of prevalence and risk factors of congenital eye malformation as well as the ability of their recognition in neonates and infants before ophthalmologic examination; (2) development of simple methods of initial examination of the organ of vision by neonatologists and paediatricians, which can make it possible to suspect some congenital pathology of the organ of vision; (3) development of principles of genetic counselling for particular groups of disorders.

Material and methods. The analysis comprised data from the Polish Registry of Congenital Malformations (PRCM) 1997-2001, including 925,162 consecutive births with 19,200 children identified and recorded because of congenital defects. Among them there were 211 children with 244 malformations of the organ of vision. The results were statistically analyzed using chi² distribution test or Fisher’s exact test.

Results and conclusions. (1) These studies have shown that the prevalence of congenital eye malformations is 2.28 for 10,000 births and it locates in the range of lower values known from other registries of malformations from other countries. Comparatively low total prevalence of congenital eye malformations, stated in the PRCM, with high prevalence of anophthalmos and low prevalence of other congenital eye malformations, suggests that the present scheme of neonate and infant physical examination in Poland is not sufficient to enable early recognition of congenital eye malformation before ophthalmologic examination. (2) Factors that increase the risk of congenital eye malformations are female sex (for Q10 and Q11 categories of malformations), birth weight below 2500g, foetal age at birth below 36 weeks, low education of fathers and presence of other birth defects (for Q11 category of malformations). (3) It is suggested to complete the scheme of neonates and infants’ physical examination by measurement of the corneal diameter with a transparent ruler, and by examination of the eyes with a pocket medical torch to assess traits that might suggest some congenital eye pathology, such as transparency of the cornea; size, shape, colour and reactions of pupils; presence of nystagmus, photophobia, fixed strabismus and oculodigital sign. (4) Significant specificity of congenital malformations of the organ of vision, frequent risk of loss of vision and imminence of extraocular symptoms, are sufficient reasons to suggest detailed regulations of genetic counseling with respect to specific needs and expectations of this group of patients.

This work was supported by the Committee for Scientific Research, Poland (grant PBZ 019-10) and Ministry of Health “Programme of Monitoring and Primary Prophylaxis of Congenital Malformations in Poland”.

(S 04)
A Kot, W Błaż, E Pszeniczna, J Rusin
THE ANALYSIS OF FACTORS INFLUENCING HIGH DETECTION RATE OF CONGENITAL HEART DEFECTS IN THE PODKARPACKIE PROVINCE.
Department of Pediatrics, Regional Hospital in Przeworsk, Poland
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Aim. To analyze the impact of methods of additional detection (screening echocardiography und pulse oximetry), regional stage referral, and watchful follow-up on high detection rate of congenital heart defects in the newborns in Podkarpackie Province.

Patients. Population of patients with congenital heart defects (CHD) enrolled from the cohort of 41832 newly born infants in the Podkarpackie Province in the years 2002-2003.

Methods. Screening echocardiography and pulse oximetry; specific stage referral system; watchful follow-up.

Results. The total detection of CHD among the newborns in Podkarpackie was 9.6/1000 and the detection of critical CHD was 1.76/1000.

Conclusions.
1. The combination of additional methods of detection, referral and follow-up resulted in the highest provincial detection rate of the CHD in newborns registered in Eurocat among Polish population.
2. Diagnostic and organizational algorithm to increase detection of CHD’s in newborns is proposed.

(S 05)
F Bianchi
THE POTENTIAL OF EUROCAT FOR EPIDEMIOLOGICAL RESEARCH
Unit of Epidemiology, CNR Institute of Clinical Physiology, Pisa, Italy
Background: During the early part of 2004 registry staff expressed anecdotal concern that they had received reports of higher than expected numbers of antenatally detected cases of gastroschisis. These concerns were also expressed by local clinicians. It was agreed that in the first instance CARIS should look at available data to establish the nature and extent of any problem.

Aim: To use routinely available registry data to:
1. Describe the current pattern and recent trends in gastroschisis in Wales
2. To compare levels of gastroschisis in Wales with other parts of the UK and Europe
3. Identify any local clusters
4. Identify potential risk factors or causes

Materials and Methods: CARIS operates a multiple-source reporting system including antenatal and neonatal sources. Relevant information from the database includes:
- Area of residence of mother
- Age of mother
- Estimated date of delivery and date of end of pregnancy
- Maternal smoking, recreational drug use, illness, and prescribed drugs
- When anomaly first detected
- Survival outcome to 1 year of life

Data quality is regularly assessed although, in the absence of a 'gold-standard', analysis of case ascertainment is problematic.

Cases of structural anomaly seen on antenatal ultrasound scan are routinely reported. When serious anomalies such as gastroschisis are detected as a local general hospital, the case is usually referred to a tertiary centre for a second opinion. In Wales there are two such centre. Cases from North Wales are referred on to Liverpool Women’s Hospital whilst in South Wales referral is made to University Hospital of Wales, Cardiff.

To ensure data quality, cases were crosschecked with those known to paediatric surgeons in South Wales. In the absence of direct links to surgeons serving North Wales, obstetricians and paediatricians in North Wales were contacted to see if they knew of any further cases.

Numbers of cases and rates of gastroschisis were analysed at All-Wales level for the years 1998-2004. Expected numbers per year were estimated (using Poisson distribution) for each of the 22 local authority areas in Wales and compared to the actual numbers for 2004. Welsh rates were compared to the most recent rates available from EUROCAT. To obtain comparative data for 2003 and 2004, data were requested from other registers within the British Isles Network of Congenital Anomaly Registers (BINOCAR).

All cases of gastroschisis known to CARIS were reviewed for possible risk factors. As no population data are available for these risk factors, cases were compared with all other cases of anomaly held by the register.

Results: Case matching with the surgeons for South Wales was complicated by issues of confidentiality. It was difficult to assess case ascertainement for 2004 as cases were being reported simultaneously to both neonatal surgeons and the register. Comparison of live born cases for earlier years suggested that case reporting to the register was complete. The register was initially of aware of one case of gastroschisis that was unknown to the surgeons. Further investigation indicated that this case had small bowel atresia alone and that the diagnosis of gastroschisis had arisen on an inaccurate clinic letter. The diagnosis was therefore removed from the database record. A general increase in cases was detected in Wales for both 2003 and 2004 compared with previous years, although these were not thought to be statistically significant. Live born rate of gastroschisis in Wales for the period 1998-2003 was 4.3 per 10,000 live births. Rates vary between years but were highest in 2003 (6.1 per 10,000 LBs, based on 19 cases). Indications were that numbers for 2004 would equal or be in excess of this figure. [By the end of March 2005 26 live born cases have been confirmed for 2004]

Overall Welsh rates for 1998–2002 were statistically significantly higher than for EUROCAT as a whole. Initial data from other British registers suggested that a non-specific rise in cases in 2003 may have also been seen in other areas of Britain, although further work was required to confirm this.

Against this background, a potential cluster of 7 cases was identified in the Bridgend County of South Wales (maximum expected = 3 per year). Unusually, none of the cases were located in the main centre of population but in the old coal
A statistically significant association with gastroschisis was found for the following risk factors.

- 77% of gastroschisis mothers were found to be under the age of 25 (OR 6.0: 95% CI 4.0 – 9.0).
- Some 10% of mothers had a history of drug abuse (OR 7.4: 95% CI 3.6 – 15.4).
- Over 60% of mothers were known smokers (OR 4.4: 95% CI 2.9-6.7).

Data to the end of 2002 showed that:

- 86% of all cases were liveborn and of these 94% survived to the end of the first year of life.
- The male to female ratio was 1.2 males to 1 female.
- Gastroschisis occurred as a single anomaly in 74% of cases.
- Conversely 26% were associated with other anomalies, commonly atrial septal defect or small bowel atresia (6% of cases). 2 cases were associated with chromosomal disorders. Interestingly a further 2 cases of gastroschisis were associated with optic nerve hypoplasia. This rare defect is not often reported, although it is known to occur more frequently in the babies of younger mothers.
- Antenatal detection was reported in 89% of cases by 24 weeks and rose to 95% by the end of pregnancy.

Discussion: Comparison of different data sources suggested that case ascertainment of liveborn cases of gastroschisis by CARIS was complete. CARIS was also able to identify other cases resulting in fetal loss that were (obviously) unknown to the surgeons. There was no way to assess the quality of CARIS data for these cases.

The rise in numbers of cases in Wales from 2003 onwards was greater than might have been expected although, so far, this rise has not been identified as statistically significant. Increases in Wales together with other areas of Great Britain are the subject of ongoing investigation by BINOCAR.

Cluster investigation falls outside both the remit and the expertise of the register. At the time that the cluster was first suspected, the process by which further investigation should take place in Wales was not clear. CARIS therefore invited interested parties to a meeting to discuss the data and agree how this matter might be taken forward. It was decided that Bridgend cases merited further investigation as a potential cluster and a separate investigation into this was undertaken, involving clinical and academic staff from the University Hospital of Wales, the National Public Health Service, Local Authority representatives, the Welsh Assembly Government and CARIS. The Investigation of the cluster of cases in Bridgend County is the subject of a separate report.

The aetiology of gastroschisis remains unclear. The risk factors identified from routinely collected CARIS data included maternal age, maternal smoking and drug abuse (although drug abuse was associated with only a small proportion of cases). This supported evidence already published in the medical literature. The association of two cases with optic nerve hypoplasia has not been widely reported in the literature.

Conclusions:

- Congenital anomaly registers can play a key role monitoring levels of congenital anomalies and in identifying clusters.
- Routinely collected register data can help the initial stages of a cluster investigation by helping to identify potential associated risk factors.
- Clearer mechanisms need to be put in place in Wales for action to be taken in the event of a possible cluster and its subsequent investigation.
- The quality of CARIS data in terms of case ascertainment for gastroschisis is good.

(S 07)
M Loane, H Dolk, I Bradbury and EUROCAT Working Group
INCREASING PREVALENCE OF GASTROSCHISIS IN EUROPE: A YOUNGER MOTHER PHENOMEMON?
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Aim: Gastroschisis is a rare abdominal wall defect commonly associated with young mothers. Recent reports have suggested an increase in prevalence despite a general decrease in the proportion of births to young women in Europe. This study aimed to investigate the increasing prevalence of gastroschisis in Europe, to assess if the increase in prevalence has been restricted to young mothers, and to identify any geographical variation within Europe after taking into account differences in maternal age.

Methods: A population-based analysis of all gastroschisis cases born between 1980 and 2002 was carried out. Twenty-five European regions in 15 countries participated in the study, covering a total of 5.79 million births. Data was extracted from the EUROCAT database which contains standardised comparable data on congenital malformations obtained from a collaborative network of European surveillance registries. All registered cases of gastroschisis that were liveborn, fetal deaths at twenty weeks gestation or more or terminations of pregnancy following prenatal diagnosis of a congenital malformation were included in the study. Cases with a chromosomal anomaly were excluded. A Bayesian analogue of ridge regression technique was used to calculate estimates of relative risk controlling simultaneously for time, maternal age, and geographical variation. Prevalence rates were standardised to the EUROSTAT 2000 maternal age structure for European births.
Results: In the years 1980-2002, 936 cases of gastroschisis were identified, giving an average prevalence rate of 1.62 per 10,000 births. Seventy-four per cent of cases were livebirths, 6% were fetal deaths, and 20% were terminations of pregnancy. The maternal-age standardised prevalence rose fourfold from 0.34 (95% CI 0.23-0.48) per 10,000 births 1980-84 to 1.33 (95% CI 1.14-1.54) per 10,000 births 2000-2002. Prevalence rose in all age groups, but with steeper trends in the younger age groups. Mothers less than 20 years of age 1995-2002 had a seven-fold risk of gastroschisis compared to 25-29 year olds. Mothers aged 20-24 years were more than twice as likely to have a baby with gastroschisis as mothers 25-29 years. The unadjusted prevalence rate varied from less than 0.7 per 10,000 births in the three Italian regions to over 3.0 per 10,000 in Mainz and three of the UK regions (Glasgow, Trent, and Wales). Controlling for maternal age, Italy (Campania, Emilia Romagna, and Tuscany) and Southern Portugal showed significantly lower age-adjusted relative risk compared to the average EUROCAT prevalence 1995-2002, varying from 0.36 to 0.60. The highest estimates of relative risk for 1995-2002 were found in Paris (France), Mainz (Germany), Finland, Wales and Trent (UK), varying from 1.7 to 2.3.

Discussion: These findings show that the prevalence of gastroschisis has increased over time in Europe, and that the increase has not just been restricted to younger mothers. There is evidence of geographical variation in risk with some regions having half the average risk and others double the average risk after controlling for maternal age variation. The UK has particularly high rates of gastroschisis especially among the younger mothers.

Conclusion: The environmental factors contributing to the increase in gastroschisis prevalence are not just restricted to mothers under twenty years of age. Geographic variation in risk may provide additional clues to the aetiology of this serious malformation.

Etiology:

(S 08)
HH Ropers
LARGE-SCALE ELUCIDATION OF GENETIC DISEASE AND IMPLICATIONS FOR HEALTH CARE
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The human genome is thought to comprise 65 to 70,000 genes of which 20 to 25,000 code for protein, but no more than 2000 of these genes have been linked to specific genetic disorders; thus, the bulk of this work still lies ahead. During the past decade, research in this area has focused on association studies in multifactorial disorders. The outcome of these studies was mostly meagre, which was generally ascribed to too small sample sizes. The alternative possibility, i.e. that many of these complex disorders are not really multifactorial but consist of a heterogeneous group of single gene disorders, has received very little attention. It is probable that the role of recessive gene defects and de novo mutations in the aetiology of ‘idiopathic’ disorders, such as sporadic cases with mental retardation and/or multiple congenital anomalies, is much higher than suspected previously, and this could also hold true for disorders that are considered as paradigms for multifactorial disorders, such as congenital heart defects or autism.

Taking mental retardation as an example, I will discuss various strategies that have been employed successfully to dissect complex disorders into separate genetic entities and to identify the underlying molecular defects in a systematic fashion. These studies, and the development of novel methods and diagnostic tools, offer great promise for the diagnosis and prevention of genetic diseases, and they may pave the way for treatment of some of them.

(S 09)
E Bocian¹, B Nowakowska¹, K Borg¹, E Obersztyn¹, I Chudoba², E Kostyk³, A Kruczek³, J Pietrzyk³, T Mazurczak¹
IDENTIFICATION OF ADDITIONAL CHROMOSOMAL MATERIAL WITH CGH AND FISH TECHNIQUES IN PATIENTS WITH PHENOTYPIC ABNORMALITIES
¹Department of Medical Genetics, Institute of Mother and Child, Warsaw, ²MetaSystems GmbH, Altlausheim, Germany, ³Department of Medical Genetics, Polish-American Children’s Hospital, Jagiellonian University, Krakow, Poland
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Approximately 30% of small supernumerary marker chromosomes (SMCs) derived from autosomes are related to an abnormal phenotype in their carriers. Because of the varying clinical outcomes attributable to the chromosomal origin of the SMCs, their detailed characterization is of great interest for reliable genetic risk estimation. SMCs may be successfully characterized only with molecular cytogenetic methods. Here we present three phenotypically abnormal patients with marker chromosomes and a case of a de novo chromosomal addition analyzed by FISH, M-FISH and
mBAND as well as with CGH techniques. We report a case of three cell lines in which two SMCs derived from chromosome 8 and 21 as well as mar(8) and double mar(21) in a patient with clinical features of trisomy 8p. A patient with mild mental retardation and mar(19) and a case of mar(22) identified in a patient with partial cat-eye syndrome (CES) is also presented. Furthermore, an additional material on chromosome Yp was revealed in a patient with severe mental retardation, hypotonia, microcephaly, short stature and dysmorphic features. Marker chromosomes were identified as der(8)(p22->q11.2:), der(21)(pter->q21.3) and der(19)(q11->q13.1). It was also found that additional material on Yp originated from chromosome Xq26->qter. Our results confirm, generally accepted and clinically useful information on the high risk of phenotypic abnormalities in the carriers of marker chromosomes containing euchromatic sequences.

(S 10)
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MAJOR CONGENITAL MALFORMATIONS AND 22q11.2 MICRODELETION
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Background: Congenital heart defects (CHD) are the most common of all human birth defects occurring in 1% of live births. Previous studies suggest that a number of patients with congenital heart disease have a 22q11.2 deletion syndrome (22q11.2 DS). Orofacial clefts are also among the most common major congenital anomalies and are included in the 22q11.2 clinical spectrum. The clinical phenotype of 22q11.2 DS is highly variable. Patients with mild clinical manifestations and apparently isolated malformation can be easily overlooked. Objective: To determine should the 22q11.2 deletion analysis become a part of the standardized diagnostic workup for CHD and orofacial clefts. Methods and patients: A consecutive series of one hundred twenty-two patients with two selected major malformations, CHD (64 patients) and orofacial clefts (58 patients) were prospectively enrolled into the study and screened for the presence of a 22q11 deletion. Detailed clinical evaluation, high resolution chromosome and FISH analysis were performed. Results: Deletions at 22q11.2 were detected in 9.4% (6/64) patients with CHD. In the subgroup of patients with conotruncal anomalies, 22q11.2 deletion was present in 17.8% (5/28) patients. None of the 58 patients with palatal abnormalities had a deletion. Conclusions: Testing is recommended for patients with conotruncal heart defects, because a substantial proportion has a 22q11.2 deletion. Deletion testing of children with other cardiac defects should be considered in the presence of additional features of 22q11.2 DS. A routine screening for the 22q11.2 deletion in children with isolated palatal anomalies may not be justified.

(S 11)
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MOLECULAR BASIS OF TOOTH AGENESIS AND OROFACIAL CLEFTS IN THE POLISH POPULATION
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Selective tooth agenesis and nonsyndromic cleft lip with or without cleft palate (CL/P) are the most common inherited craniofacial disorders in man. Despite this, little is known about the genetic defects responsible for these complex conditions. To date, many polymorphisms and several mutations correlated with these developmental malformations have been described. However, the results of the reported associations largely depend on the population and the geographical area of the world. The MSX1, PAX9, TGFα and IRF6, belong to the main candidate genes whose mutations are responsible for tooth agenesis as well as CL/P.

The aim of the report was the analysis of the main candidate genes responsible for tooth agenesis and orofacial clefts in a group of patients from the Polish population, in an attempt to explain the reason of these common developmental disorders.

The main results of the study of the candidate genes responsible for tooth agenesis were identification of three novel heterozygous mutations located in MSX1 and PAX9 that might cause severe oligodontia. One of them, a 151A>G transition, found in a highly conserved paired box sequence of PAX9 was the first de novo mutation described in this gene, suggesting that PAX9 might be a good candidate gene for an isolated form of tooth agenesis.

Analysis of candidate genes responsible for orofacial clefting revealed an association between two polymorphic variants of TGFα (BamHI, OR = 1.878; RsaI, OR = 1.627) and cleft lip, with or without cleft palate. As opposed to other populations, it was shown that polymorphic variants of MTHFR, IRF6, RARα and PAX9 were not associated with this common developmental disorder.
Our results provide the first step to identification of genes contributing to the aetiology of selective tooth agenesis, as well as cleft lip with or without cleft palate in the Polish population, and might provide an insight into better diagnosis and prevention of these common inherited disorders.

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(R 12)
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MOLECULAR PATHOGENESIS OF HIRSCHSPRUNG DISEASE – THE SIGNIFICANCE OF POLYMORPHISMS OF RET GENE
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Hirschsprung disease (Hd) is a congenital disorder, characterized by the absence of intestinal ganglion cells. Various genes are included in the aetiology of Hirschsprung disease. Diverse models of inheritance, co-existence of numerous genetic disorders and detection of numerous chromosomal aberrations together with involvement of various genes confirm the genetic heterogeneity of Hd. Recent advances show that the aetiology of Hirschsprung disease focuses on the meaning of RET gene. There are plenty of different mutations in this gene. No mutation is fully penetrant and they have varying effects on the length of the aganglionic segment of the intestine. The aim of our study was to analyse single nucleotide polymorphisms (SNP) of RET gene in several exons. To test how the Hd phenotype may be affected by the presence of genetic variants, we compared the molecular results with clinical and long-term follow-up data. The study group comprised 120 patients. Molecular DNA analyses were performed in 60 cases. There were almost 4 times more affected males than females. Family history for Hd was investigated only in four patients. We found a short segment of aganglionic gut in 64% and ultra-short segment in 16%, and long-segment in 20% of all patients. The 135A and 1296A and 2712G RET variant has been shown to be strongly associated with the Hd phenotype. Seven patients died in the endstage F508 was found, in other 5:of the illness, in two of them homozygous mutation patients genetic analysis was not performed. We have demonstrated that RET haplotypes containing these polymorphisms play a role in the aetiology of Hd. In the nearest future a genetic test and demonstration of mutation in genes involved aetiology of Hd could determine the severity of the clinical picture of Hd and the risk for Hd patient’s family.

(E 13)
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The assumptions and purpose of the study: 1. Defining the commonest phenotypic features of chromosome 18 trisomy. 2. Analysis of congenital abnormalities types observed in patients from an examined group. 3. Analysis of characteristic symptoms occurring during prenatal screening which may suggest the appearance of chromosome 18 trisomy. Material and methods: This study included 75 neonates born in ICZMP (Polish Mother’s Memorial Hospital Research Institute) in the years 1993–2004. Clinical diagnosis of chromosome 18 trisomy was verified every time by cytogenetic analysis based on cultivating peripheral blood lymphocytes. In some cases Edwards Syndrome was diagnosed prenatally. Material for the examination was obtained by amniocentesis or cordocentesis. Abnormalities were diagnosed on the basis of physical examination, echocardiogram, radiological and ultrasound imaging. Results and discussion: In analyzed group of 75 born- alive neonates with Edwards Syndrome (in the years 1993-2004) there were 54,6% (41) of females and 45,3% of males (34). It was found that the commonest abnormal features that might suggest the chromosome 18 trisomy were: intrauterine growth retardation (retardation observed in 4th-9th week)-95,8% (70 neonates), polyhydramnion 89% (65 neonates) and congenital abnormalities concerning more than one organ 98,6% (75 neonates). Congenital heart defect was the commonest congenital abnormality in examined group 91% (67 neonates). Conclusions: 1. Coexistence of polyhydramnion, intrauterine growth retardation and presence of congenital abnormalities may suggest the possibility of chromosome 18 trisomy occurrence in neonate. 2. The commonest complex of congenital abnormalities in chromosome 18 trisomy- Edwards syndrome, according to analyzed material, are congenital heart diseases (91%) (VSD, iAVC). 3. Other abnormalities occurring with congenital heart defects in Edwards Syndrome in examined group were: digestive tract abnormalities (31%), CNS abnormalities (27,7%).
Aim: Determination of priority risk factors of newborn babies with congenital malformations in Kyiv Region.

Volume and Methods. During 1999-2003 1206 newborns with congenital malformations were registered in Kyiv Region in the network of the Special State Genetic Monitoring Program. The group of healthy carried babies (975) was considered the control group. Risk factors influence was estimated by odds ratio calculation with 95% confidence interval.

Chronic infectious diseases were the priority factors of congenital malformations appearance risk. Chronic infectious diseases among women and men increased the probability of abnormal child birth (OR=2.96 with CI 1.98-4.44 for women and OR=6.62 with CI 2.48-19.20 for men).

Chronic extragenital diseases among women increased the probability of their giving birth to babies with congenital malformations (OR=1.79 with CI 1.43-2.25), including endocrine diseases (OR=1.27 with CI 1.00-1.60) and bad habits (smoking, drinking) (OR=2.00 with CI 1.47-2.71).

Occupational hazards among future parents also increased risk of their giving birth to babies with congenital malformations (OR=1.45 with CI 1.03-2.06 for women and OR=1.36 with CI 1.06-1.75 for men).

Conclusion. The determined risk factors are guided factors so there is a good possibility for primary prophylaxis of congenital and inherited pathology among newborns.

Aim. Quantitative signal detection is a commonly used method to detect new adverse drug reactions (ADR) in spontaneous pharmacovigilance reporting systems. Since the occurrence of birth defects after maternal drug exposure can be seen as a specific type of ADR, we performed a survey on maternal drug use in the 1st trimester and the occurrence of birth defects in the offspring in our population based registry of congenital malformations.

Methods. We selected 3286 cases born between 1981 and 2003. Birth defects were coded according to ICD9 and ICD10. Drugs were coded according to the ATC-codes. We investigated combinations of 51 categories of malformations, not part of a chromosomal or monogenic disorder, with >= 10 subjects present and 60 groups of drugs with >= 10 exposed subjects present. As controls we used 669 subjects with a recognised chromosomal or monogenic disorder. For malformation-drug combinations with >= 2 exposed cases we measured the possible disproportionality by calculating the Chi2 and the proportional reporting ratio (PRR) with a 95% Confidence Interval (CI).

Results. In total 718 malformation-drug combinations had >= 2 exposed cases. For 87 combinations an increased risk was found with a p-value<0.05. Of these combinations 4 had a p-value < 0.01 and a lower PRR >=3: omphalocele x M01 (antirheumatic drugs), p=0.001, PRR=16.7, 95%CI=4.9-24.3; anorectal atresia x D01 (antifungals for dermatological use); p=0.004, PRR=12.4, 95%CI=3.3-15.3; malrotation of intestines x A06 (laxatives), p=0.004, PRR=10.7, 95%CI=3.3-14.4; microcephaly x J01EA (trimethoprim and derivates), p=0.005, PRR=44.6, 95%CI=4.2-50.7. Also ASD x N05BA01 (diazepam) had a p-value of 0.001, but the PRR could not be calculated because there were no exposed controls. This method detected also the previously documented risk of exposure to fatty acid derivates (N03AG) and spina bifida (p=0.031, PRR=12.2, 95%CI=1.7-13.7).

Discussion. The combinations of drugs and malformations that are disproportionately present in our database may reveal signals of potential teratogenic drugs. However, the most strong signals are not described in literature before and the drug groups are heterogeneous. Therefore these results have to be interpreted carefully and critically. They have to be further evaluated, for example in an other database or by using analytic study designs.
RECREATIONAL DRUG USE: A MAJOR RISK FACTOR FOR GASTROSCHISIS?

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Aims: This study was designed to test the hypothesis that the risk of gastroschisis is positively associated with the use of recreational drugs in the weeks immediately following conception and to validate data collected at maternal interview concerning recreational drug use during pregnancy using maternal hair analysis.

Methods: A matched case control study was conducted in three UK health regions over the period January 2001 to August 2003. For each case, three live born controls were selected, matched by initial intended place of delivery, region and maternal age. Case note review and maternal interviews were used to collect information about risk factors for gastroschisis. Hair was collected for analysis to validate interview data concerning recreational drug use. Conditional logistic regression analysis was used to estimate the mutually adjusted odds ratios for gastroschisis associated with any recreational drug use and class A or B drug use. These estimates were revised using results from the hair analysis.

Attributable risks were calculated.

Results: The adjusted odds ratio (aOR) for gastroschisis associated with first trimester use of any recreational drug during early pregnancy was 2.20 (95%CI 1.13 to 4.26) and class A or B drugs was 3.59 (95%CI 1.36 to 9.47). These statistically significant excess risks were increased to aOR 2.56 (95%CI 1.34 to 4.91) and aOR 3.82 (95%CI 1.58 to 9.22), respectively, when additional class A or B drug users, identified at hair analysis, were added to the analysis. The estimated attributable risk for gastroschisis of Class A or B drug use during early pregnancy was 6.7% (95%CI 1.7 to 23.4).

Conclusions: There is a significantly increased risk of gastroschisis associated with the use of recreational drugs in early pregnancy. The addition of class A or B drug users identified at hair analysis increased this risk further. However, although mothers who took Class A or B drugs in early pregnancy had an almost four fold risk of a gastroschisis pregnancy the estimated proportion of gastroschisis cases that were attributable to such drug use was less than 7%.

MATERNAL OBESITY AND CONGENITAL ANOMALIES: TEMPORAL CHANGE IN BMI IN EMILIA ROMAGNA, ITALY.


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Aims: Obesity (defined as body mass index BMI $\geq$ 30kg/m$^2$) is increasing across Europe. The International Obesity Task Force (IOTF) estimate that there are a billion adults overweight and over 300 million obese people worldwide. Maternal obesity adversely impacts pregnancy outcome and has been associated with an increased risk for some types of congenital anomalies. Given the evidence from the literature regarding maternal prepregnancy obesity as a risk factor for some congenital anomalies and the increase in obesity reported for the general population a preliminary study was conducted using the IMER registry of congenital anomalies database to investigate if maternal prepregnancy obesity in mothers giving birth to babies with congenital anomalies is increasing over time and whether the prevalence by type of anomaly differs in obese and underweight mothers compared to the normal weight mothers.

Methods: The IMER registry of congenital anomalies covers the Emilia Romagna region of Italy: a population of 4 million inhabitants and around 25,000 births per year (http://www.unife.it/imer). IMER joined the EUROCAT network in 1980 (EUROCAT). As well as the variables collected for the EUROCAT database IMER runs a local database of other local variables.

The maternal prepregnancy weight and height of mothers is routinely recorded on the IMER Congenital Anomalies notification form and entered in the IMER database. These parameters were used to calculate the body mass index (BMI) of non diabetic mothers giving birth to cases where BMI = kg/m$^2$. BMI was classified as:

- Underweight BMI <18
- Normal BMI 18.5-24.9
- Overweight BMI 25 to 29.5
- Obese BMI $\geq$ 30 kg/m$^2$

Regression analysis was carried out on the maternal BMI per year over the 20 year period 1982-2002 to see if there is an increasing trend over time. This was compared to a limited database of control mothers (1982-1995). Mean height and weight by year was also plotted separately.

Further analysis of the data to establish if there are differences in OR by BMI (following Watkins et al.) was not conducted due to the lack of control data after 1995. The malformations recorded were divided into three groups: underweight mothers, normal weight mothers and overweight and obese mothers. The number of cases by type of malformation in each of these groups was calculated as a percentage and plotted graphically in order of the frequency in the normal weight mothers.
Results: The classification of mothers giving birth to babies with congenital anomalies by prepregnancy BMI category was conducted on the 9519 cases reported to IMER in the 20 year study period. 1787 cases were excluded as height or weight data was missing. Of the remaining 7732 cases the mothers were: Under weight (BMI <18.4) 628 cases (8.1%), Normal weight (BMI 18.5-24.9) 5729 cases (74.1%), Overweight (BMI 25 to 29.5) 1045 cases (13.5%) and Obese (BMI ≥ 30kg/m²) 330 cases (4.3%). From regression analysis of maternal prepregnancy BMI from 1982 to 2002 of cases and controls, the trend line shows maternal prepregnancy BMI to be increasing over time. When treated separately, both height and weight graphs showed an increase over time. In the study period mean height increased by 2.5cms while mean weight increased by 4.5 kgs. For certain types of malformation obese mothers represented a higher than expected percentage while underweight mothers a much lower than expected percentage (anencephaly, encephalocele, TOF). Gastroschisis and HLH on the other hand were higher than expected in underweight mothers and lower in obese women.

Conclusions: This preliminary study shows the trend for maternal prepregnancy BMI to be increasing over time in mothers giving birth to babies with congenital anomalies in Emilia Romagna whilst the control group seems to be remaining stable. However, caution is required in interpreting this data as limited data on controls was available. Even if we ignore the control trend it seems that in common with the general population in many countries, the sub group of maternal prepregnancy BMI in Emilia-Romagna is increasing with time. A change over time in both height and weight of mothers is seen. Underweight mothers seem to be more at risk for some congenital anomalies (eg. gastroschisis, HLH) and obese mothers less at risk than the normal weight mothers. The opposite is true for anencephaly, encephalocele and TOF. Given that the literature has reported BMI as a risk factor for congenital anomalies attention should be payed by registries to gaining this data. Obesity like maternal age and smoking needs to be taken into account as a variable/confounder in interpreting data on congenital anomalies. Maternal prepregnancy BMI is easy to calculate with the two variables height and weight normally recorded when a pregnant women checks in for antenatal care. A pregnancy in an overweight or obese women should be monitored with caution given the data in the literature regarding the lower detection rates by ultrasound of congenital malformations. Hence whilst maternal obesity represents a higher risk factor for congenital anomalies the probability of a prenatal diagnosis is lower. This needs to be taken into account in the interpretation of prevalence data as live births may be higher to obese mother due to lack of prenatal diagnosis and terminations.

As shown from this preliminary study control information is needed in order to calculate odds ratios and counsel on increase risk of malformations for obese women.

A large scale European study is recommended the results of which could lead to support in primary prevention.

among women in childbearing age. It was established that the incidence rate of NTD in newborns in Poland due to Program activities should lower by 35% to year 2005 and by 70% to year 2010. The Program is based on an informational and educational campaign directed to health professionals, women in childbearing age and secondary school students. Due to considerable differences among local communities the Program has been implemented through a network of provincial program coordinators from the Sanitary Epidemiological Stations responsible for the management of field program activities coordinated by the Central Program Office.

During the period of Program financing over 100 thousands educational books and booklets for medical doctors, nurses and midwives were edited, over 1 million educational materials (leaflets and posters) for women in childbearing age and secondary school students were distributed and over 2000 trainings for medical doctors, nurses and midwives were organized. Over 1 million secondary school students participated in special educational program for youth “I can now help my baby to be healthy”. The Program has established its www pages with educational materials available.

Effectiveness of the Program has been assessed by changes in NTD mortality and morbidity rates, changes in women’s knowledge, attitude and behaviour concerning folic acid supplementation and changes in the amount of tablets containing 0,4 mg of folic acid sold.

During 1996-2002 years infant mortality caused by anencephaly decreased by 54% (from 24.8 to 11.3 per 100 000 live births) and infant mortality caused by spina bifida - by 59% (from 9.8 to 4.0 per 100 000 live births).

The repeated country-wide studies have shown, that although the percentage of non-pregnant women taking vitamin tablets containing folic acid did not increase (24.0% in 1999, 24.8% in 2003), 10.6% of women pregnant during the interviews in 1999 and 17.4% in 2003 began folic acid supplementation before pregnancy.

The first monovitamin tablet containing 0.4 mg of folic acid appeared in sale in 1999. Since then the sale trend of the tablet has been constantly increasing.

(S 20)
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PREVENTION OF NTDs WITH FOLIC ACID SUPPLEMENTATION AND FOOD FORTIFICATION IN BRITISH COLUMBIA, CANADA: OVER A 10 YEAR EXPERIENCE IN A ‘LOW INCIDENCE AREA’
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Folic acid (FA) supplementation has been shown to help prevent neural tube defects (NTDs). The protective effect is greater in high incidence areas compared to low incidence areas. Although, FA supplementation has been well studied, the effectiveness of food fortification with FA had not been studied prior to initiation of Public Health interventions. This study reports on the NTD incidence in British Columbia over a 10 year period, from 1992-2000.

Methods: This is a population based, retrospective chart review of prospectively ascertained cases evaluated in health centers in B.C. as well as cases reported to B.C. Health Status Registry. All NTD affected newborns, stillborns, therapeutically aborted fetuses and spontaneous losses > 20 weeks born to mothers residing in B.C. were ascertained. The study time period was Jan. 1, 1992 through Dec. 31, 2002. Cases and anomalies were confirmed using medical records from multiple sources.

Results:

<table>
<thead>
<tr>
<th>Years</th>
<th>FA initiatives</th>
<th>NTDs LB + SB + TABs</th>
<th>Total B.C. Births</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992 – 93</td>
<td>Pre-FA recommendation</td>
<td>113</td>
<td>92,511</td>
<td>1.22/1000</td>
</tr>
<tr>
<td>1994-96</td>
<td>FA supplements Pre-food fortification</td>
<td>146</td>
<td>140,431</td>
<td>1.05/1000</td>
</tr>
<tr>
<td>1997-1998</td>
<td>FA supplements, Transition to fortified flour &amp; cereal products</td>
<td>89</td>
<td>86,875</td>
<td>1.02/1000</td>
</tr>
<tr>
<td>1999 – 2002</td>
<td>FA supplements, FA fortification</td>
<td>163</td>
<td>163,688</td>
<td>0.99/1000</td>
</tr>
</tbody>
</table>

Discussion: Recommendations for FA tablet supplementation were initially issued by the U.S. CDC and PHS in 1992. Similar recommendations were issued in Canada in 1993, at which time it was estimated that 10% of the population were already taking multivitamins. In March 1996 the U.S. FDA approved FA fortification of enriched grain products, with fortification with 0.15 mg/100 gm grain starting Nov 1, 1998. Many U.S. firms started fortifying products shortly after March 1996. Health Canada approved a similar fortification plan, to be initiated by November 1, 1998. Because of Free Trade, U.S. products fortified with FA would have been available as early as March 1996. During the period of 1999-2000 all flour products as well as other food products would have been available to B.C. women. There was an unexpected increase in 1999 of 62 NTDs/42,040 births (1.47/1000) which otherwise obscures the overall decline in the NTD incidence.
An overall decline of 37% in the NTD incidence of B.C. was observed as a result of FA initiatives. B.C. is a relatively low incidence area. Based on FA supplement intervention studies in China, we would anticipate that there would be a less dramatic reduction in B.C. compared to higher incidence areas of Canada. Newfoundland and Labrador [Crane et al, 2001] reported a decline from 4.6/1000 in 1992-1996 to 1.2/1000 in 1998, a 74% reduction. Quebec reported a decline of 32% from 1.89/1000 in 1992-97 and 1.28/1000 in 1998-2000, [DeWals et al., 2003].

Conclusion: FA supplements and food fortification have been effective in reducing the NTD incidence in British Columbia and elsewhere in Canada. It is anticipated based, on the China study, that FA interventions are unlikely to reduce the population incidence below 0.6/1000.

(S 21)

PA Boyd, E Garne, C DeVigan
EUROCAT SURVEY OF POLICIES FOR PRENATAL SCREENING FOR FETAL ANOMALY OPERATING IN EUROPEAN COUNTRIES
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With recent advances in prenatal screening methods and with improved resolution and expertise at ultrasound scanning the questions of which screening test to use and when to offer ultrasound scans in pregnancy are difficult ones to answer. The availability of different resources, termination of pregnancy laws and social and cultural factors are important issues which vary in different countries. Different policies have been developed in different countries and in different areas within countries. This study aims to “map” the current state of prenatal diagnosis in countries in Europe which are members of EUROCAT.

A questionnaire was developed to explore current (as in 2004) policies on prenatal screening for malformations (Down’s syndrome and structural anomalies) and termination of pregnancy for fetal anomaly. The questionnaire was sent to a previously nominated register leader from each country who was asked to contact all other register leaders in their country about local policies. Responses have been received from fourteen out of 18 leaders contacted.

Results.

Screening for Down’s syndrome -National Policy:
Nine /14 countries had some national policy / guidelines in place in 2004. The policies were different for each country – some used a maternal age cut off alone to offer a diagnostic test to older mothers, others used a mixture of maternal age screening and mid trimester (Triple) screening and/or nuchal translucency screening with or without maternal serum biochemistry. The policy for some countries was for nuchal translucency or mid trimester maternal serum screening to be offered to all women. One country had a screening policy based on a detection rate i.e. a screening test should be offered that had a detection rate for Down’s syndrome of >60% for a false positive rate of <5%.

Of the five countries with no official national policy for prenatal screening, four offered a variety of maternal age screening, first and second trimester screening although for some women this is on a private basis.

Indications for prenatal cytogenetic diagnosis:
In eleven / 14 countries maternal age (usually ≥35 years) was given as an indication for prenatal cytogenetic diagnosis; in two this was only on offer (for Down’s syndrome) after a screening test had been performed. One country did not offer prenatal cytogenetic diagnosis. Other indications for prenatal cytogenetic diagnosis were similar in all 13 countries i.e. it was offered to translocation carriers, family history of chromosome anomaly and after ultrasound diagnosis of major malformations or certain soft markers.

Screening for structural anomalies by ultrasound scanning:
Ten / 14 countries had a national policy / recommendation regarding fetal ultrasound scanning in place in 2004. These policies recommended an anomaly scan at 18-22 weeks with in most countries additional (morphometric) scans at 10-14 weeks and 28 – 32 weeks.

Termination of pregnancy for fetal anomaly (TOPFA):
There is very wide variation in the policies for TOPFA. In one country termination of pregnancy is illegal. The gestation limit for TOPFA varies from 12 weeks gestation to no limit. For most countries the limit is 22 – 24 weeks. In some countries later TOPFA is allowed if permission is sought from a special committee.

(S 22)

J Stańczyk, K Niewiadomska-Jarosik, D Tomecka, B Kierzkowska
CARDIOLOGICAL PRENATAL DIAGNOSTICS: A FIFTEEN-YEAR EXPERIENCE
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Aim: The aim of the study was to present our own experience in prenatal diagnostics of congenital heart defects (CHD) and arrhythmias in fetuses of women with a higher risk of delivering child with a pathology of cardiovascular system.

Material and methods: We retrospectively analyzed 1862 fetuses of women of the higher risk group. 1980 prenatal echocardiographic examinations were performed. CHD was diagnosed in 152 fetuses and arrhythmia in 114.

Results: 8% (152/1862) of fetuses from the studied group had CHDs. The most common conditions were Atrio-Ventricular Septal Defect (AVSD: 34 fetuses, 22.3%), Hypoplastic Left Heart Syndrome (HLHS: 19 fetuses-12.5%), Ventricular Septal Defect (VSD: 16 fetuses, 10.5%) and Aortic Stenosis (AS: 10 fetuses, 6.6%). 18 (11.8%) patients with CHD died in utero, and 9 (5.9%) shortly after birth. 65 (42.7%) underwent cardiosurgical correction after birth. In fetuses with arrhythmias (114/1862, 6%) the most common conditions were extrasystoles (71 fetuses, 62.3%), supraventricular tachycardia (21 fetuses, 18.4%) and complete atrioventricular block (22 fetuses, 19.3%). 12 (10.5%) patients with arrhythmia died (9 in utero, 3 shortly after birth): 10 fetuses and 1 newborn died of complete atrioventricular block and congenital heart defect. All fetuses with supraventricular tachycardia were treated pharmacologically, 18 (85.7%) with good effect.

Conclusions:
1. Fetal echocardiography enables early diagnosis of the CHD and fetal arrhythmias.
2. Prenatal diagnostics of the CHD enables referral of the pregnant women to the Health Center, where cardiological and cardiosurgical treatment is possible.
3. The coexistence of the fetal complete atrioventricular block and CHD is associated with poor prognosis.

(S 23)
P Sieroszewski, E Baś-Budecka, M Perenc, J Suzin
ULTRASOUND DIAGNOSTIC SCHEMA FOR DETERMINATION OF INCREASED RISK FOR CHROMOSOMAL ANEUPLOIDIES IN FOETUS IN THE FIRST HALF OF PREGNANCY
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The aim of the study was to develop early ultrasound diagnostic schema for the determination of increased risk for foetal chromosomal aneuploidies.

Material and methods. The study comprised population of 1318 pregnant women divided into 2 groups: 1255 women with normal course of pregnancy and 63 women with diagnosed fetal abnormalities. There were 34 cases of chromosomal abnormalities (trisomy 21, 18, 13, triploidy, unbalanced inversion 9, deletion 16) and 29 cases of structural malformations. Ultrasound scans were performed with Hitachi EUB 525 LI digital scanner. The estimation of range normal values for the nuchal translucency (NT) measurement between 11 and 13 weeks and nasal bone length (NB) measurement between 12 and 20 weeks (correlation with biometric parameters – CRL and BPD) was performed. The results obtained from the pool of normal pregnancies established the basis for calculating the range of normal values. The measurements of NB and NT showed a linear value increase in the pregnancy course. For the nuchal translucency measurement correlated with CRL (38 – 85 mm) the values increased from 1.29 mm to 1.86mm. There was a similar tendency for the nasal bone length which increased from 1.88mm to 3.69mm. The following test characteristics (correlation to CRL) were registered: NB – sensitivity 60%, specificity 98%, positive predictive value (PPV+) 43%, negative predictive value (NPV-) 98.9%. Assuming the test outcome means presence or absence of the nasal bone in the ultrasound scan sensitivity was 40%, but specificity 100%; NT – sensitivity 63.6%, specificity 98.2%, PPV+ 38.9%, NPV- 98.2%; NT + NB – presents similar characteristic to the NB or NT alone - sensitivity 55.6%, specificity 98.6%, PPV+ 50%, NPV- 98.9%. The normal values of the markers in correlation with the biparietal diameter BPD (20-55 mm) were observed as follows: nuchal translucency NT from 1.62mm increases to 2.87mm, nasal bone length NB from 2.52mm to 7.29mm. The following test characteristics for chromosomal aberrations markers (correlation to BPD) were noted: NB - sensitivity 68.4%, specificity 97.4%, PPV+ 56.5%, NPV- 98.4%; NT - sensitivity 73.9%, specificity 97.9%, PPV+ 54.8%, NPV- 99.2%; NT + NB - sensitivity 94.7%, specificity 98.9%, PPV+ 90%, NPV- 99.7%. The “genetic sonogram” protocol for the structural defects detection was analysed: sensitivity was 80%, specificity 100%, PPV+ 100%, and NPV- 99.7%.

Conclusions:
1. Two new biometric parameters: nasal bone length (NB) and corrected nuchal translucency thickness (NT) are useful markers for fetal abnormalities, especially for chromosomal aberrations.
2. High predictive values of the diagnostic schema for the detection of aneuploidies and structural defects recommend its use in correlation with the biparietal diameter (BPD).
3. The proposed schema is an effective algorithm for prenatal diagnostic characterised by high prognostic values.
4. Possible implementation of the schema could have an influence on the decrease of the invasive procedures rate, which could minimise the rate of miscarriages as complication of the amniocenteses.
In Ukraine as well as in other post-soviet countries, there is no experience of effective activities of parental organizations. Besides, their number is very limited. Thus, planning the Ukrainian-American Birth Defects Program (UABDP) activities, we made maximum encouragement of education of parents with birth defects children and their joining together to be among our priorities. This task was assigned to 6 informational-resource centers (RC), created in the UABDP frames.

The key elements of an RC are: trained information officers who are English-competent and knowledgeable of electronic information sources and web-technology; trained medical/clinical experts cognizant of BD, genetics and teratology; access to printed, electronic or web-based information resources; access to national and international consultants; RC staff located in major pediatric health care centers who, therefore, implicitly partake in RC activities; easy access to RC by professionals and the public through the extension of operating hours beyond standard working hours; electronic publication and dissemination of information resources developed by local authors; partnerships with medical and other teaching/training programs.

Today, RCs serve as a center for creation of new parental organizations and development of newly created. Using the existing resources parents get free access to contemporary information about new methods of treatment and rehabilitation of their children, establish contacts with similar parental organizations in Ukraine and abroad. Moreover, using foreign NGO’s experience parents initiate and stimulate state administrative bodies to create modern facilities for social rehabilitation of children.

That’s why, we consider RCs to be the essential element stimulating parents of birth defects children for creation of parental support groups and their effective work.
Posters:

**Epidemiology:**

(P 01)

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**EPIDEMIOLOGY OF CLEFT LIP AND PALATE IN EUROCAT REGISTRIES**

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Understanding the etiology of birth defects is relevant for developing treatment and preventive strategies. Most birth defects have an underlying genetic basis and many different approaches have been used to identify disease genes for single gene and genetically complex birth defects. Cleft lip and palate are common congenital anomalies; more than 400 single gene causes of clefts of the lip and/or palate are listed in the Online Mendelian Inheritance in Man catalogue. Other etiological factors include chromosomal rearrangements, genetic susceptibility to teratogenic exposure and complex genetic contributions to gene-environment interactions. The intensive effort of current research has not revealed major risk factors for human clefting probably reflecting a more complicated etiology of the oligogenic model originally proposed. It is therefore encouraging that several important risk factors have been recently identified directly from human analysis. Interestingly, this has been achieved using syndromic cleft lip with or without cleft palate (CL/P) patients with additional phenotypic features. Gene and environment research should seek to find the risk of CL/P associated with different populations and ethnic groups. Integration of genetic information into epidemiological studies can help identify links between etiological factors whilst different prevalence in different populations indicate direction for genetic research. A descriptive epidemiological study of CL/P in Europe has been performed in order to give a background of cleft lip and palate prevalence and evaluate differences that can be attributed to etiological factors (genetics, environmental or both)

**Methods:** Data from 23 centres in 14 European countries of the European Surveillance of Congenital Anomalies (EUROCAT) network of regional registers were considered for the study period 1980-2000. Recorded cases included live births, stillbirths and induced abortions following prenatal diagnosis. Cases of cleft lip (CL) and cleft lip and palate (CLP) were classified as the following: isolated- no other anomaly present; associated- two or more unrelated anomalies present. This group was further subdivided in recognized conditions (chromosomal, monogenic, sequences, environmental) and multiple congenital anomalies (MCA) of unknown origin.

**Results and discussion:** Prevalence. A total of 5,449 cases of CL and CLP were ascertained from 6,003,797 births. The prevalence of oral cleft (9.1x10,000; 95CI 8.8-9.3) corresponds with published data. A significant difference in the prevalence rate of CL/P among European centres both for the total cases (chi-square 393.75 df=22 p<0.0001) and for the isolated (chi-square 359.58 df=22 p<0.0001) was found. 6 registries (Hainaut-Namur, Odense, northern Netherlands, Strasbourg, Saxony-Anhalt, Styria) located in central-north Europe show higher prevalence than the European average. High prevalence of cleft in northern Netherlands has been previously reported.

**Isolated/associated:** Our study confirms published data that isolated CL/CLP presents more frequently (3,860 cases =70.8%) than cases associated with other malformations. Cases with CL only were 1,582 out of 3860 (41%) among isolated cases and 414 out of 1,589( 26%) when associated. The proportion of CL with respect to CLP was 41% (1,582/3,860) amongst isolated and 26% (414/1,589) in cases with more than one malformation. The 1,589 with other associated anomalies presented a total of 5,974 malformations (ratio of malformations to malformed 3.76). 970 cases (17.8%) were MCA and 619 (11.4%) recognized conditions of which 455 were related to chromosomal anomalies (in particular 252 cases of trisomy 13) and 164 (3.0%) were syndromes.

**Sex.** A male excess was found, as previously reported in Caucasian populations (SR1.70; 3400/2002) (in 47 cases the sex was either unknown or not determined) higher among isolated cases (SR1.87;2,504/1,342) and in severe isolated cases (CLP)(SR1.92, 1,494/777 ).

**Live births/stillbirths/terminations:** As expected the proportion of serious malformations is higher in stillbirths. 203 cases (203/5,449; 3.7%) were stillbirths of which 71% (144/203) reported CLP with associated anomalies.

In the study period (1980-2000) 508 pregnancies were terminated (508/5,449; 9.3%): 479 of the associated cases and 29 of the isolated cases. Among the associated cases, termination was performed in 47.4% for the presence of a chromosomal anomaly, in 42.0% for other defects (multiple congenital anomalies) and in 10.6% for a syndrome. In only 16 cases (0.3%) the malformation was reported in spontaneous abortions.
Maternal age. The overall mean maternal age was 28.8 years: the mean maternal age for isolated cases was 28.5, for associated 29.4 and for chromosomal 32.1 years. In agreement with the literature maternal age does not seem to be a factor of importance for these defects.

Conclusions: High frequencies of CL/CLP as reported in the literature highlight its importance from the health service point of view. Birth defect registries represent an important tool in etiologic studies of congenital anomalies. A precise definition of the malformation and the recognition of specific associations should help the subdivision of cases in etiologically related groups. The possible association with other defects, syndromes and chromosomal anomalies emphasise the need for thorough investigation in prenatal and postnatal life.


Introduction. The Emilia Romagna region of Italy has around 4 million inhabitants and, in recent years, a rapidly increasing immigrant population. In order to understand the demographic changes in the region and their possible impact on the interpretation of results from the Emilia Romagna congenital anomalies register (IMER) a study was set up with the following objectives:

- quantify the importance of immigration on the reference population of the IMER birth defects registry.
- identify for major groups of malformations the prevalence in the population with immigrant mothers compared to the total population in E-R
- identify the underlying risk factors
- create effective monitoring within the registry
- propose specific health policy initiatives to help at risk groups and predict resource needs

The preliminary results of this on-going study are reported here.

Method: IMER (Indagine delle Malformazione nel Emilia Romagna) was set up in 1978 to investigate congenital anomalies (CA) in the Emilia Romagna region of Italy http://www.unife.it/imer. It is a member of the EUROCAT network of CA registries. http://www.eurocat.ulster.ac.uk/. The establishment of common ascertainment criteria in the EUROCAT network enables comparison of prevalence and the analysis of the geographic variation of major birth defects. Denominators and population data were obtained from the Emilia-Romagna region and ISTISAN and ISTAT. An analysis of demographic statistics for the E-R region 2001-2003 was carried out along with the identification of IMER cases 2001-2003 with mothers of non Italian origin. The immigrant sub group was compared to the total denominator birth population and data from the literature to identify factors that may be of importance in understanding prevalence of congenital anomalies.

Results and discussion. Immigration in Emilia Romagna is a factor not only from one country or geographic area but from different countries and ethnicities outside of the European Community. The total population of ER in the 2000 census was around 4 million. The number of registered foreigners is rapidly rising from 81,200 in 1997 to 130,300 in 2000 and registered foreigners now represent 3% of the population. The importance of the immigrant population increases when live births and women of reproductive age are considered. In 2001 the IMER registry covered 24,425 births of which 2986 had one or both parents with non Italian citizenship (12.2%). In 1999, 36.3% of the Italian female population were of reproductive age (18-44) compared to 80.4% of the immigrants. Whilst female immigrants are 1.8% of the total population this rises to 4% if only women of reproductive age are considered Congenital anomaly prevalence data.
Five countries contributed 50.7% of the immigrant mothers giving birth in Emilia-Romagna in 2003: Morocco (957 births) Albania (666) Tunisia (427) China (407) and Romania (326). 101/245 cases (41.2%) of congenital malformation cases recorded by IMER in the study period were to mothers from these countries. The overall prevalence of congenital malformations in Emilia Romagna for the study period was 1.77%, (1447/81642). We can estimate a birth prevalence of 245/16,500 or 1.48% for non-Italian mothers confirming previous data that the overall prevalence of congenital anomalies is not higher in the immigrant population than the total population. Analysis by type of anomaly is underway.

Maternal age. In recent years births to mothers over 35 in Emilia Romagna has continued to rise arriving in 2000 at 21.7%. In 2001 mean maternal age was significantly lower in immigrants (27.7 years) than Italians (31 years) P<0.0001. Maternal age is an important risk factor in congenital anomalies.

Consanguineous marriages/ micro populations
Marriage to a close relative is common practice in many Asian populations and has been shown to continue in migrant populations. In the study period in 28 cases the parents were related with 82% of the cases recorded being immigrant couples. In addition migration is not a random occurrence. Rights to abode are given to relatives of those already resident in the country while often people from the same village migrate to cities where friends and relatives are established. In 1999, requests for residence permits motivated by ‘presence of family’ was given by 8.7% of males, 47% of females (25% total). Hence a micro population can be formed with a limited genetic pool leading to a higher prevalence of a specific congenital anomaly. An example is the high incidence in Bradford (UK) of children with visual impairment of Pakistani origin.

Socio-economic factors. The motivation for migration to Italy is often economic. 65%-84% of males and 40% of females with residence permits in 1998 gave the motivation for their presence as work. Hence socio-economic factors are an important consideration. Socio demographic factors such as fathers/mothers employment status, type of work, zone of residence, level of education have been widely used in the literature in assessing risk of CA and are regularly recorded in the IMER register. These factors permit future analysis.

Health status, access to health services and attitudes to abortion.
Maternal illnesses prior to pregnancy and family illnesses are recorded by IMER allowing the assessment of general health. Illness and drugs during pregnancy are also recorded.
Ability to access the health services in a timely manner by immigrant women who are pregnant or plan a pregnancy may be difficult due to linguistic barriers, lack of knowledge of the services available (egg genetic counselling) or illegal status. This may lead to late or no prenatal diagnosis which together with religious beliefs may affect attitudes to abortion. The level of total abortions among immigrant women in Italy has risen sharply and in 2000 was 16% of the total.

Conclusions. A birth defects registry needs to be able to deal with the factors that may affect congenital anomaly prevalence in a changing population. Coding of country of origin of the mother and period of residence is now routinely recorded by both the Regional health authority for all births and the IMER congenital malformation registry for cases enabling analysis of the data collected.

The priority for public health in understanding birth defects in an immigrant population needs to be high where immigrant populations are growing. Whilst differences in risk factors have been identified immigrant mothers do not seem to be more at risk for birth defects overall. The study will continue to monitor immigrant mothers and analyse other risk factors such as parity and socio-demographic factors. An analysis by type of congenital anomaly is underway.

(P03)
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THE RESULTS OF BIRTH DEFECTS MONITORING IN NEWBORN IN RUSSIA
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OBJECTIVE: Analysis of total prevalence and prevalence of selected types of birth defects in Russian register during four years 2000-2003.
METHODS: The original data were collected in population-based regional registers and then were sent to Federal Birth Defects Register. Only live and stillbirths were recorded in monitoring register.
RESULTS: The monitoring during period between 2000-2003 covered 2,381,336 newborns from 36 regional registers. This number included 44337 infants with one or more birth defects all types. So the total rate was 186.19 per 10000 newborns. The mean rate of 21 selected types of birth defects was 61.7 per 10000. There are significant regional differences in reported BD rates.
The rate of selected birth defects varies between registers from 103.4 in Kaluga region to 36 in Tyumen region. Many factors influence on regional BD prevalence: methodological problems, geographical and ethnic differences as well as other factors. In spite of this the structure of BD is similar in different regions. The most common birth defects group is
malformation of musculoskeletal system (including limb defects) and connective tissue (23%), congenital defects of cardio-vascular system (23%) and birth defects of urogenital system (11%). The most common types of BD are hypospadias (12.28 per 10000 birth), Down syndrome (9.44 per 10000) and the rare congenital malformations are epispadias (0.17), bladder exotrophy (0.22). We investigated some epidemiological characteristics of different types of BD including associations with maternal age, infant sex, birth weight and gravidity.

CONCLUSIONS: The obtained birth defects prevalence in different Russian regions will be used for BD surveillance and for evaluation of effectiveness of BD prevention.
Background: Along with considerable progress in prenatal testing for Down’s syndrome (DS), socioeconomic differences in its use have been documented. However, the impact of these differences on the proportion of DS cases diagnosed prenatally, or the live birth prevalence of DS has not been studied adequately.

Aim: To assess, using population-based data, socioeconomic differences in prenatal diagnosis of DS and their impact on live birth prevalence of DS.

Materials and Methods: Based on data for 1,433 cases of DS and 3,731 malformed controls from the Paris Registry of Congenital Malformations during the period 1983-2002, we assessed maternal age-adjusted effects of maternal profession and geographic origin on prenatal diagnosis, continuation of pregnancy after prenatal diagnosis, and total and live birth odds of DS. Statistical analyses included fractional polynomials to determine the optimal strategy for adjustment of maternal age.

Results: Maternal profession and geographic origin had significant effects on the probability of prenatal diagnosis, and continuation of pregnancy after prenatal diagnosis of DS. We also found increasingly higher odds of a DS live birth for lower maternal profession groups. Women without a profession had more than a two-fold increase in the odds of a DS live birth (Adjusted Odds Ratio, 2.4, 95% CI, 1.7–3.3) as compared with women in the highest professional category. In contrast, we did not find any disparities in the age-adjusted total odds of DS.

Conclusion: The increasing use of prenatal testing accompanied by persistent socioeconomic differences in its use has created disparities in the prenatal diagnosis and thereby live birth prevalence of DS, a congenital malformation whose overall risk does not vary by socioeconomic status.

( P 07)

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A HEREDITARY COMPONENT OF BIRTH DEFECTS OF SKIN BLOOD VESSELS IMMINENT TO CHILDREN

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It is believed that environmental component is the main cause for appearance of birth defects of skin blood vessels (DBV). DBV’s genetic determination is being discussed. Today, hemangiomas and vascular malformations are considered to be sporadic cases, but some cases of autosomal dominant and autosomal recessive types of succession are considered to have different nature. DBV can be a component of complex inheritable syndromes. Our goal was to define frequency of appearance and to estimate hereditary components of appearance of DBV among children population of the city of Kiev.

Statistics and methods. During the period between 1999 and 2003 all cases of DBV were registered by birth units (the total number of these locally registered cases was 534) or by outpatient units where cases were input into family medical genetic histories (the hospital register counts 144 such cases).

The result. The frequency of DBV among newborn babies is 5,1 per 1000 that counts 22,2% of overall cases of birth defects. The share of sporadic isolated cases of vascular pathologies is 84,7%. 15,3% cases of DBV are components of inheritable syndrome. Frequency of complications in family anamnesis of DBV among relatives of 1st to 3rd degrees is 17,4%, that means a need of medical supervision over such cases and medical genetic consultations to be given to patients.

In the 2% of cases autosomal dominant type of succession was detected. To diagnose sporadic mutations in family related cases it is necessary to use cytogenetic methods and DNA diagnostics.

(P 08)

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MATERNAL AGE AS A RISK FACTOR FOR ISOLATED CONGENITAL MALFORMATIONS IN CHILDREN IDENTIFIED BY THE POLISH REGISTRY OF CONGENITAL MALFORMATIONS

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The number of pregnancies in mothers over the age of thirty has markedly increased in many developed countries. Maternal age is an important risk factor for chromosomal aberration syndromes in children, but its effect on the prevalence of isolated congenital malformations is largely unknown.

Goal: To assess the prevalence rates of the isolated congenital malformations in relation to the mother’s age.

Methods: 13,976 cases of children aged 0–2 years with isolated congenital malformations were analyzed. All cases were identified from the population of 1,018,646 infants live-born between 1998 and 2002 in 12 regions of Poland as documented in the Polish Registry of Congenital Malformations.

Results: In California a reported hydrocephalic birth rate of 353 and a microcephalic birth rate of 491 to approximately 1 in 10,000 live-births. The prevalence of isolated congenital heart defects was also higher in mothers aged 30 years or more (49.09 per 10,000 live-births in the 30-34 year old group; 49.90 in the 35-39 year old group; 60.30 in mothers over 40).

Younger maternal age (24 years of age or less) was a risk factor for the isolated gastroschisis (3.98 per 10,000 live-births in mothers 19 years old and under and 2.09 in the 20-24 year old group). There was no association with maternal age for following congenital malformations: neural tube defects (anecephaly, encephalocoele, spina bifida), microcephaly, hydrocephalus, congenital hydronephrosis, renal agenesis or hypoplasia, cystic kidney disease, diaphragmatic hernia, omphalocoele, hypertrophic pyloric stenosis, oesophageal atresia, small intestine atresia or stenosis, large intestine atresia or stenosis, anal atresia or stenosis, reduction defects of upper and lower limbs, deformities of foot, congenital dislocation of hip, polydactyly, or hypospadias.

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(P 09)

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HYDROCEPHALY AND MICROCEPHALY IN CHILDREN BORN BETWEEN 1998-2002 IN POLAND AND CALIFORNIA – EPIDEMIOLOGICAL STUDIES.

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Introduction: The purpose of our study is to compare the epidemiological data on Microcephaly and Hydrocephaly in live-born infants (0-12 months) born in area of Poland covered by the PRCM and the state of California in 1998-2002. This project is a collaboration between the Polish Registry of Congenital Malformations (PRCM) and the Californian Birth Defects Monitoring Program (CBDMP).

Methods: The data from these two registries have been compiled using the registries’ individual databases and is combined into an extended appendix which shares the following features; sex, birth date, birth order, birth type, birth weight, duration of pregnancy, father’s and mother’s age, father’s and mother’s education, previous pregnancies, and accompanying malformation. We have compared our estimates with these, as well as, with various other published estimates.

Results: In California a reported hydrocephalic birth rate of 353 and a microcephalic birth rate of 491 to approximately...
Aim: Nijmegen breakage syndrome (NBS; OMIM *251260) is a rare human autosomal recessive DNA repair disorder characterized by microcephaly, immunodeficiency, radiosensitivity, and a very high incidence of cancer. The more frequent occurrence of this condition in Poland than in other populations allowed us to undertake intensive longitudinal studies.

Material and methods: The NBS diagnosis was verified by mutation analysis in all 89 patients identified to date (March 2005), whose clinical data are collected in the Polish NBS registry evaluated at the Department of Medical Genetics CMHI. Polish patients constituting approximately half of all registered NBS patients worldwide are all homozygous for the common mutation 657del5 in exon 6 of the NBS1 gene (founder effect).

Results and Discussion: Collecting such a unique group of patients allowed us to characterize phenotypic pleiotropy and the natural history of the disease. One of the most important features of NBS is unprecedentedly high incidence of lymphoid malignancies, when compared with healthy individuals and other cancer-predisposing diseases. To date, about 50% of patients have developed a malignancy by the age of 20 years, of which 90% were of lymphoid origin.

Conclusions: 1) The number of identified NBS cases is clearly lower than expected from a relatively high carrier frequency of the common germline mutation in our population (0.6%). 2) The malignant manifestation of NBS is mainly B-cell lymphomas, in which DNA double-strand breaks (DSB) are produced by V(D)J recombination and hence, NBS is a good model for understanding the mechanism of DSB-derived tumorigenesis.

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(P 11)

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NEURAL TUBE DEFECTS PREVALENCE IN THREE REGIONS OF WESTERN POLAND IN 1997-2000

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Introduction: Geographical differences in NTDs prevalence exist. In Poland until now prevalence rates for NTDs were estimated only in epidemiological studies of small populations. The health care planning and NTD prophylaxis efficacy assessment require precise estimates of the prevalence rates.

Aim: To assess prevalence rate of different types of neural tube defects in 3 regions of Western Poland in years 1997 – 2000.

Methods: Based on the data from the Polish Registry of Congenital Malformations (PRCM) the prevalence of different types of the neural tube defects has been calculated for years 1997 to 2000 for three regions of Western Poland (Kujawsko-Pomorskie, Lubuskie and Wielkopolskie). Standardized reporting questionnaires on congenital malformations were used as a primary information source and were entered into the Registry database.

Results: In years 1997 to 2000 the PRCM registered 302 children with an NTD born to mothers living in the area of interest. The prevalence of neural tube defects in all three regions was 10.81 cases per 10 000 live- and stillbirths (95% confidence interval: 9.63-12.10). In years 1997-2000 the prevalence of NTDs in Kujawsko-Pomorskie Region was 9.42 per 10 000, in Lubuskie – 9.79 and in Wielkopolskie – 11.97. The prevalence for specific types of the NTDs in all regions was as follow: anencephaly – 2.36 (95% CI 1.83-3.01), spina bifida – 7.30 (6.34 – 8.38) and encephalocele – 1.15 (0.78-1.62).

No significant differences of the prevalence between regions and between the consecutive years were noted.

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Birth defects monitoring based on international standards was implemented in two oblasts of western region under the Ukrainian-American Birth Defects Program support in 2000. Since 2002 the Program was joined by three more oblasts of Ukraine – one western oblast and two southern regions.

There were 73406 livebirths in three western oblasts during 2002-2003. During the same period 154 cases of neural tube defects (NTD) were registered among livebirths, stillbirths, and induced and spontaneous abortions. The prevalence of NTD was 154/73406 or 2.1 per 1000 livebirths. Among them there were 139 cases of spina bifida and anencephaly (prevalence 1.9 per 1000).

In two oblasts of southern region of Ukraine there were 54382 livebirths during 2002-2003. During the same period 77 cases of NTD were registered in these oblasts. The prevalence was 77/54832 or 1.4 per 1000 livebirths. Amount of spina bifida and anencephaly was 69 cases (prevalence 1.3 per 1000).

One should note that the NTD data are consistent during several years. Besides, the contrast between NTD prevalence in western and southern regions of Ukraine was pointed out. Possible reason for this is the difference between human diet of population. This fact must be further studied.

Totally there were at least 146 cases of spina bifida and anencephaly in 2002-2003 in western and southern regions of Ukraine which could be prevented by means of folic acid intake.

The birth defect monitoring system existing in five oblasts of Ukraine allows monitoring changes of NTD prevalence during implementation of folic acid fortification in Ukraine and accomplishing follow-up care for recurrent NTD cases in women of the risk group.

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THE EPIDEMIOLOGY OF HYPOSPADIAS IN WALES - 1998-2002
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Aim: The aim of this work is to describe the epidemiology of hypospadias in Wales using best available data from the Welsh Congenital Anomaly Register (CARIS).

Objectives: To ensure that CARIS data is of the highest possible quality in relation to hypospadias by:
- Making an initial assessment of case ascertainment and completeness
- Where possible accessing new data sources available to CARIS
- Making an assessment of the improvement in data quality as a result of accessing new data sources.
- To describe the epidemiology of hypospadias in Wales (1998 – 2002) based on all available data.

Methods: The population under consideration is the Welsh population of live births as reported by the office for National Statistics (ONS). Inclusion criteria were defined as all cases of hypospadias diagnosed in children whose mothers are normally resident in Wales at the time of birth with dates of end of pregnancy in the years 1998 – 2002. Controls used were all other live born males with a congenital anomaly recorded on the CARIS database and with a date of end of pregnancy in 1998 – 2002. Data was obtained from inpatient records from 2 of the 3 centres that carry out repair surgery for hypospadias for Welsh babies.

Results: Using Dolk’s estimate of the prevalence of hypospadias in Europe (30 per 10,000 total births) the ascertainment of cases of hypospadias held by CARIS register was calculated to be 64% at the start of the study. This rose to 82% with the addition of cases identified from surgical repair centres. In addition the proportion of unspecified cases fell by 12%. Inpatient data in South Wales contributed 84 cases previously unknown to the register for the 5-year period 1998 – 2002. The prevalence of hypospadias in Wales for the years 1998-2002 is now reported as 24.5 per 10,000 total births. Whilst several factors, such as birth weight and parental age discussed in the literature showed an indication of association with hypospadias, statistical significance was not reached in this study. Comparing current data with data published almost 40 years ago suggests that the prevalence of hypospadias may have risen by over 50% during this time period in parts of South Wales.

It has been possible to estimate repair rates and age of repair. Over 50% of balanic cases are known to have had repair surgery carried out. The mean age of repair was between 2 and 3 years old.

Discussion: It became apparent in organising this study that there are few independent sources of data that a congenital anomaly register can call on to help with ascertainment and completeness. There were issues of confidentiality and ethics which made gaining access to data from Liverpool, (covering patients from North Wales), impossible in the time period available. It was thought that because hypospadias is a relatively common congenital anomaly and unlikely that many mild cases would have been reported to the register, there was the potential to make a large difference to the register’s overall ascertainment by using inpatient data. This proved to be the case. The main reason for this being that codes for hypospadias in ICD10 are condition specific and all cases undergoing repair surgery should normally have an inpatient episode coded at the centres of repair surgery. Because the inpatient database only holds an ICD10 code it may not be so helpful for other conditions that do not have a specific ICD10 code. The inpatient database was also helpful in improving the coding specificity on cases already known to CARIS. A pragmatic approach was adopted that a more specific code already held by CARIS would be preferred to a less specific one from inpatient data, but cases with a more specific code on inpatient data would be preferred to an unspecified code held by CARIS. This policy affected the specificity of ICD 10 code for 12% of cases. It has been CARIS’ experience that those cases of anomaly that are serious, life threatening or requiring immediate treatment at birth, with perhaps admission to a special care baby unit or neonatal intensive care, are generally well reported across Wales. Those cases that are not apparent at birth, or for which there is no immediate treatment available tend to be less well reported. Babies delivering at term with no other anomaly other than hypospadias are likely to be discharged from hospital soon after birth and not reported to CARIS. Looking at inpatient data, when such cases return at 12 months or later for repair surgery is the only way these cases have been found. For mild cases born at term and not requiring corrective surgery or where parents decide not to choose the option of surgery, these cases are probably being lost to CARIS.

Prevalence of hypospadias in Wales is now approaching rates quoted in the literature. The decision by CARIS to ignore the exclusion of glanular hypospadias in 1999 has been supported by the EUROCAT special report on the surveillance of hypospadias. However, published data from EUROCAT still excludes glanular hypospadias but includes unspecified cases. This means that a register with a high number of unspecified cases will report a higher rate based on EUROCAT criteria but a register with low numbers of unspecified cases is likely to show a lower rate, because many unspecified cases are likely to be glanular. Comparing current data from Wales with other EUROCAT registers shows that there are 10 registers with a higher rate than Wales. The proportion of unspecified cases from these registers is not known. A significant proportion of cases have not had a full data set completed and this has undoubtedly weakened some of the results in this study.

Conclusions: Multiple source reporting is essential for a register to obtain good ascertainment and the identifying of potentially new sources of data needs to be continuously explored. CARIS should review hypospadias again in another 5 years to establish evidence in Wales for a current temporal trend. A complete dataset on cases registered with CARIS is needed to support epidemiological findings in the literature.

(This work was submitted as part of a dissertation for a Masters in Public Health degree at the University of Cardiff, Wales – 2004.)
Gastroschisis is a life threatening malformation defined as a defect of the abdominal wall located to the right of the intact umbilical cord. Increased incidence of gastroschisis in some populations has been reported recently. An association with young maternal age, protein-zinc deficiency and intrauterine exposure to vasoactive factors (e.g. cyclooxygenase inhibitors, decongestants, recreational drugs, cigarette smoke) and carbon monoxide was also suggested.

To verify some epidemiological and etiological findings on gastroschisis the data concerning autopsies of children with congenital malformations performed in our institution from 1981 to 2000 was reviewed. Out of 1062 autopsies with congenital abnormalities 19 cases of gastroschisis have been found. The incidence has not significantly changed in the analysed period (1981-1990 vs. 1991-2000, p>0.05). The sex ratio was M:F = 9:10. In 5 cases gastroschisis was accompanied by other malformations such as intestinal atresia (4 cases), cardiac defects (2 cases), and accessory spleen (1 case). The mean maternal age was 21.42 years. Eight mothers were from the urban areas. Two mothers suffered from common cold during the first trimester of the pregnancy. However, no drug administration or exposure to chemicals during pregnancy was revealed.

The results partly confirmed some general trends of gastroschisis, especially young maternal age. Unlike many world reports, no differences in the malformation incidence in the last two decades were observed. There was no direct evidence of exposure to drugs and chemicals, however, in 11 women the first trimester of gestation came out in autumn and winter. Therefore, either mild infections or administration of popular OTC medications cannot be completely excluded, despite their absence in medical records.

Objectives: Several factors are reportedly associated with an adverse outcome in gastroschisis, including mode of delivery, in utero diagnosis, type of closure, concurrent anomalies, intestinal atresia, and necrotizing enterocolitis (NEC). Since 1991 we have treated in the NICU Polish Mother’s Health Center 66 patients who had gastroschisis. We analyzed their data to identify variables associated with increased morbidity and mortality.

Methods: A retrospective study of all patients with gastroschisis treated in the NICU was performed. The characteristics of the survivors and nonsurvivors, admitted to NICU in 1991-1996 and 1997-2004 were compared. A logistic regression analysis was performed, with survival as the dependent variable, and the following parameters as independent variables: in utero diagnosis, mode of delivery, gestational age and birth weight, type of closure, intestinal atresia, and development of necrotizing enterocolitis.

Results: Mean gestational age was 36.8 weeks, mean birth weight 2349g. The overall mortality rate was 16.7%. In 1991-1996 the mortality rate was 45.5%, and in 1997-2004 – 2.38. There were no differences in gestational age, birth weight and mode of delivery, method of closure, or presence of intestinal atresia between the survivors and nonsurvivors and between the newborns admitted to our NICU in 1991-1996 and 1997-2004.

Only presence of necrotizing enterocolitis and postoperative complication necessitating reoperation, prenatal diagnosis and birth in the tertiary center correlated with mortality in the logistic regression analysis.

Conclusions: Mode of delivery, birth weight and gestational age, do not appear to correlate with survival in infants with gastroschisis. Only the presence of major postoperative complications, development of necrotizing enterocolitis, prenatal misdiagnosis and birth outside of the tertiary center was associated with increased mortality. The type of delivery had no influence on either morbidity or mortality.
Gastrochisis is a serious condition involving a defect in the anterior abdominal wall. Prevalence is reported to be rising throughout the developed world. Wales has one of the highest prevalence rates of gastrochisis among the EUROCAT registries. During early 2004 there was a rise in the number of babies born with gastrochisis. This rise appeared to be focused within Bridgend Borough County.

Aims: To identify whether there was a local cluster of gastrochisis in Bridgend County Borough, to identify causes, instigate appropriate public health action and make recommendations.

Materials and Methods: A multidisciplinary group was set up to investigate the apparent cluster. Data from the CARIS registry was used to describe the background pattern of gastrochisis in Wales. A case was defined as “Babies / fetuses with gastrochisis whose mothers were normally resident in Bridgend County Borough and who had an expected date for the end of pregnancy during 2004.” A literature review was undertaken to inform the investigation. Information on cases and mothers of cases was acquired from patient notes. Clinicians conducted interviews with mothers to find epidemiological links. Information on the physical environment was sought from multiple agencies.

Results: Seven women in Bridgend County Borough conceived babies closely related in time who developed gastrochisis during 2003. Five occurred in the more sparsely populated North of the County. There appeared to have been a general increased risk in gastrochisis in the previous year, but nonetheless, the cases in Bridgend were considered a local cluster. Many risk factors previously described were evident among mothers in the cluster, e.g. low body mass, poor diet, and smoking in pregnancy. Although no factor was identified it is noted that the time in question was a hot dry summer, with high PM10 measurements across the UK. There is no nearby landfill site; however, the area is near a large industrial site.

Discussion: This investigation adds to the growing body of evidence that gastrochisis tends to occur in clusters. It is unusual for cluster investigations in the community to come up with positive results. No factor was identified that could explain this cluster; however, there was evidence of behaviour in this group of young pregnant women that can pose a risk to health (e.g. poor diet, smoking). A number of issues were highlighted during the course of the investigation including concerns between the boundary between research and public health investigation, sharing of information, and related ethical issues, including the storage and testing of biological samples taken for other purposes. Relations with the media were of particular note. The distinction between the risk factors associated with gastrochisis in general, and the cause of this local cluster in particular was an important distinction during the investigation. The lack of a local policy or protocol for dealing with such clusters was highlighted. The role of the media is discussed.

Conclusion: An investigation of a local cluster of gastrochisis highlights the need for ongoing research into the cause of this condition. Although no cause for the cluster investigation raised several questions relating to possible aetiology. Investigations of clusters of non-communicable disease are not as common among public health services as those of communicable disease, appropriate local guidance can be helpful in overcoming issues that arise during an investigation.

(P 17)

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THE OCCURRENCE OF CONGENITAL MALFORMATIONS IN THE REGION OF ŁODŹ ON THE BASIS OF THE DATA FROM POLISH REGISTRY OF CONGENITAL MALFORMATIONS
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Aim: The main objective of this research was assessment of the time of diagnosis, type and incidence of congenital malformations (CM). Moreover, it includes and analyses data about the period of pregnancy of mothers whose children suffer form CM.

Material and methods: This retrospective analysis covers the results of a questionnaire of 1587 children admitted to the Polish Registry of Congenital Malformations in the region of Łódź.

Results: CM were diagnosed in the prenatal period among 13.2% of children, while in 68.3 % by the 7th day after birth. Distressful is the fact that 14.4% of cases were not subjected to prenatal USG (1 or 2 USG examinations were carried among 16% of pregnant women, while 3 or more in 52.8%). Most often (33.5% of cases) CMs were diagnosed between the 33rd and 37th week of pregnancy. Predominantly CMs occurred as congenial heart disease (26.4%), malformation of musculoskeletal (17.7%) and genital (12.5%) systems. Male patients with CMs constituted a clear majority and accounted for 57.2% of cases. The percentage of detected CMs (rate per 1000 live births) increased substantially – from 7.1% (in 1999) to 20.8% (in 2004, due to the fact that more questionnaires were filled in). Generally, (60%) children with CM were born of mothers aged 21-30 years.

What raises attention is the low percentage of women taking folic acid (11.8% - 24.4%).

Conclusions: 1. In spite of availability of USG examinations, prenatal diagnostic of CM is insufficient.
2. Congenital heart disease was the most frequently diagnosed type of congenital malformations.
3. Children with CMs were often born of mothers aged between 21-30 years.
4. Low percentage of women taking folic acid outlines the necessity of propagation of preventive treatment of neural tube defects.

(P 18)

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Purpose: The aim of our paper was a retrospective comparative analysis of incidence of congenital malformations in newborns born in the years 1989-1992 and 1999-2002 in the I Division of Gynecology and Obstetrics, Medical University of Lodz.

Materials and Methods: The research took into consideration 421 newborns born alive who were diagnosed in their perinatal period as having a congenital malformation. The group examined consisted of 284 newborns born in the years 1989-1992 and 137 newborns born in the years 1999-2002. During the analysis 9 groups of congenital malformations were discerned, depending on the organ or system affected, and their incidence was related to the date of birth. The diagnosis of a malformation after delivery was made on the basis of subject examination as well as additional examinations such as ultrasonography, radiography, echocardiography and genetic examination.

The research was conducted retrospectively on the basis of the case records of newborns’ development and case records of their mothers (years 1989-1992), as well as taking into account data from the Polish Central Register of Inborn Developmental Anomalies (years 1999-2002).

The statistical analysis was made by means of the Fisher’s test (the level of statistical significance was accepted as p < 0.05) and the model of regression by Poisson.

Results: Among 9134 newborns born alive in the years 1989-1993 – 284 (3.11%) were born with a congenital malformation. In the years 1999-2002, among 6680 newborns 137 (2.05%) were born with congenital malformations. This means that within 10 years we have observed a significant decrease of the number of newborns with congenital malformations (p=0.017) born in I Division of Gynecology and Obstetrics, Medical University of Lodz.

In the years 1989-1992 the predominant anomalies were malformations of the skeletal system (6.6 cases/1000 newborns born alive), congenital heart diseases (5.1 cases/1000 newborns born alive), malformations of the central nervous system (4.8 cases/1000 newborns born alive) and defects of skin and soft tissues (4.6 cases/1000 newborns born alive).

In the years 1999-2002 the most frequent were congenital heart diseases and malformations of the urinary-sexual system (each: 4.3 cases/1000 newborns born alive) as well as malformations of the osteoarticular system (3.3 cases/1000 newborns born alive).

In the years 1999-2002, in comparison with the earlier period, there was an increase of the risk of occurrence of malformations in the urinary-sexual system (IR=1.42), but this difference is not statistically significant. However, there was a statistically significant decrease of the number of multiple malformations (p=0.017), malformations of the central nervous system (p=0.02), malformations of the osteoarticular system (p=0.004) and also defects of skin and soft tissues (p < 0.001).

Generally, it should be stated that the risk of occurrence of congenital malformations in newborns during both periods decreased (IR=0.66), and in the years 1999-2002 there was also a significant drop concerning the incidence of congenital malformations (p=0.017).

Discussion: Congenital malformations are one of the most important problems of contemporary neonatology. They are also listed among the basic reasons causing deaths of fetuses and newborns. The Central Polish Register of Inborn Developmental Anomalies has been run since 1 July 1995 and it is an attempt to introduce a systematic solution of the problem of malformations in the whole country. The incidence of congenital malformations has been on a stable level and there has been observed an increase. The incidence of inborn malformations quoted by different authors varies, depending on the period of research, the kind of population and the kind of research methods: from 1.5 to 10%.

In our material, the frequency of newborns born alive with malformations was on the same level (3.11% - 2.05%). However, during the period of 10 years the number of newborns born with inborn malformations decreased.

Conclusions:
1. In relation to the previous 4-year analysis, the incidence of congenital malformations in our material has undergone a significant decrease.
2. The developmental malformations discovered most often in newborns in our material in the years 1999 – 2002 were congenital heart diseases and malformations of the urinary-sexual system.

(P 19)
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ANALYSIS OF MORTALITY DUE TO CONGENITAL MALFORMATIONS IN NEWBORNS AND INFANTS BORN IN POZNAN BETWEEN 1998 AND 2004
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Aim of the study: The aim of the study is the analysis of deaths from congenital malformations among newborns and infants born in Poznan in years 1998-2004.

Material and methods: The analysis covered deaths from congenital malformations in children aged 0-12 months who were born and died in the city of Poznan.
The underlying cause of death was established according to WHO recommendations given in Vol. One of the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems.

Results and discussion: Congenital malformations are a major medical and social problem. Prevalence of congenital malformations is estimated to be around 1-7%. In Poland the prevalence is from 1.5% to 3% depending on time and region. Epidemiological research indicates that congenital malformations are one of the major causes of death amongst newborns and infants.

Mortality rate for congenital malformations in Poznan in the years 1998-2004 does not show any particular tendencies and varies between 3.4% in 1998 and 2000 and 1.0% in 2003.

Within the seven years analyzed there were 81 infant deaths where congenital malformations were the underlying cause. Cardiovascular, CNS and unspecified malformations were given as the most frequent causes of death. It must be noted, however, that diagnoses on death certificates are usually vague. In our analysis we found that most deaths concerned newborns with low birth weight. Amongst the infants who died, the female sex was prevalent.

Conclusions:
1. Amongst the infants who died from congenital malformations, those with low birth weight prevailed.
2. The most frequent congenital malformations were those of the cardiovascular system, CNS and multiple malformations.

(P 20)
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NEWBORNS AND INFANTS MORTALITY IN THE CENTRAL POMERANIA REGION OF POLAND (1983 – 1997) DUE TO CONGENITAL MALFORMATIONS
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Contiguous series of newborns and infants’ mortality notifications of 2027 cases from 1983 and 1997 from the area of Central Pomerania Region have been retrospectively analysed. Congenital malformations, prematurity, infections and respiration distress syndrome have been analysed during the successive years of observation. Small defects and anomalies which were not life threatening were excluded.

Results: At the beginning, infection/RDS were more frequently diagnosed as a cause of death (34 %) and only 16% of congenital defects cases. As opposite, at the end of investigation birth defects were more frequent (38.3% vs. 22.3 %). Among birth defects, Congenital Hearth Defects (41%) were more frequent reasons for newborns and infants’ deaths in the period 1987 – 1997.

Conclusions:
2. During this time, due to decreased mortality caused by other factors, the number of deaths caused by birth defects shifted to the first place.
3. The mortality rate due to congenital malformations was comparable to data from other regions of Poland and from literature.
4. The main cause of children’s death in the Central Pomerania Region were Congenital Heart Defects (41%)
5. The mortality rate due to congenital defects being the result of trisomy 21 was at the fifth place.

(P 21)
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Congenital malformations are one of the most important and still current problems of contemporary medicine, especially perinatology, and they occupy high places among the death causes of newborns and infants. Registration of cases is the best way of monitoring inborn defects in population.

The aim of this thesis was:
2. Analysis of selected factors that could relate to the occurrence of inborn development defects in infants.
3. Identification of administrative districts with a higher incidence of inborn defects in the Warmia-Mazury province.

Creating a map of inborn defects in the Warmia-Mazury province with a specification to districts.

This concerns inborn development defects in infants which were registered at the Polish Registry of Congenital Malformations (PRWWR) under the supervision of the Provincial PRWWR Unit, whose coordinator in the area of Warmia-Mazury was the author of this thesis (personally supervising the completeness of the registered cases). The PRWWR registers congenital defects detected in children up to two years of age as well as defects in babies who were born dead and recognized prenatal defects. Incidence and the kinds of congenital malformations in aforementioned voivodships were defined regarding the sex of the baby with inborn defect, the body mass at birth, fetal age, the age and education of parents, the place the mother’s residence (city – countryside).

Results. The incidence of congenital malformations of newborns was defined in the Olsztyn province at the rate of 172.3/10000 (cases to number of births) (1998) and in the Warmia-Mazury province 156.5/10000 (1999-2000). The most frequent defects in the Olsztyn province (1998) were muscular-skeletal defects, cardiac defects, and chromosome aberration syndromes, and in the Warmia-Mazury province (1999-2000) defects of sexual organs before muscular-skeletal and cardiac defects.

Among babies with inborn defects in the Warmia-Mazury province between 1999 and 2000, boys outnumbered girls (54.3%). The analysis of incidence of specific groups of inborn defects when related to the sex of the baby with an inborn defect shows that only in the case of development defects of sexual organs there is a significant statistic difference with regard to boys and girls (it occurs more often with boys). No major statistical difference in the incidence of inborn defects was discovered regarding mother’s education and place of residence (city – country). However, there was a proven relation between low fetal age and small body mass and high incidence of inborn defects.

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(P 22)

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Advances in medicine have contributed to reduced mortality among infants, principally due to improved chances for survival of immature newborns. As a result, congenital have become the second cause of infant death in industrialized countries.

It was therefore decided to start studies among children born in Western Pomeranian District in the ears 1998-1999 to estimate prevalence and type of congenital defects.
All newborns born in our voivodeship between Jan. 1st 1998 and Dec. 31st 1999 were enrolled. Data on congenital defects were collected from all neonatal and infant wards with the aid of special charts. Analysis allow only children with large defects.

Among children born in these period in Western Pomeranian District 19.37/1000 live born infants were have many types of congenital defects. The most frequent were defects of cardiovascular (7.07/1000) and musculoskeletal systems (6.69/1000), followed by chilognathopalatoschisis (1.76/1000), gastrointestinal tract (1.1/1000), nervous system (1.84/1000), sex organs (3.08/1000) and urinary system (1.22/1000).

High prevalence of congenital defects among children born in Western Pomeranian District point at the propriety of continuation studies to estimate the prevalence and for efforts to establish and estimate factors predisposing to congenital defects in the future.

(C P 23)

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ASSOCIATED MALFORMATIONS IN CHILDREN WITH LIMB REDUCTION DEFECTS

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Infants with limb reduction defects (LRD) often have other associated congenital defects. The reported incidence and the types of associated malformations vary between different studies. The purpose of this investigation was to assess the prevalence and the types of associated malformations in a defined population. The prevalence and types of associated malformations in infants with LRD were collected in all livebirths, stillbirths and terminations of pregnancy between 1979 and 2002 in 320,810 consecutive births in the area covered by our population based registry of congenital anomalies. LRD were classified according to the « Classification of limb defects (Am.J.Med.Genet.1998; 77: 430-441).

Of the 246 LRD infants born during this period, 58.1% had associated malformations. Associated malformations were more frequent in infants who had upper limb reduction defect (63.2%) than in infants with lower limb reduction defects (48.4%). Malformations in the cardiac system and in the central nervous system were the most common other malformations, 15.2% and 10.6% of the associated anomalies, respectively, followed by anomalies in the genital system (10.1%), in the renal system (6.8%), and in the digestive system (6.3%). There were 16 (6.5%) cases with chromosomal abnormalities, including 8 trisomies 18, and 2 22q11 deletion, and 56 (22.8%) nonchromosomal dysmorphic syndromes. There were no predominant dysmorphic syndromes, but VA(C)TER(L) association. However numerous dysmorphic syndromes were registered including, among them, the following : EEC, OFD, Klippel-Trenaunay-Weber, OAVS, CHARGE, Townes Brocks, Moebius, De Lange, SLO, hypoglossia-hypodactyly, amniotic band, De Lange, Rubinstein Taybi, Fanconi, TAR, Roberts, Holt-Oram, and fetal diethylstilbestrol. Seventy one (28.8%) of the cases were multiply, non syndromic, non chromosomal malformed infants. Prenatal diagnosis was performed in 48.8% of dysmorphic syndromes with LRD, whereas prenatal ultrasonographic detection was only 23.9% in cases with isolated LRD. The overall prevalence of associated malformations, which was more than one in two infants, emphasizes the need for a thorough investigation of infants with LRD. A routine screening for other malformations especially cardiac, central nervous system, urogenital system, facial clefts, and digestive system may need to be considered in infants and in fetuses with LRD.

(P 23)

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COEXISTENCE OF URINARY TRACT ABNORMALITIES WITH OTHER MALFORMATIONS FROM THE POLISH REGISTRY OF CONGENITAL MALFORMATIONS IN THE POMERANIAN REGION FROM 1999 TO 2001

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Urinary tract congenital defects often coexist with other types of malformations. The prevalence of this phenomenon has been estimated to be between 10 - 23%.

The aim of this study was to analyze the coexistence of urinary tract congenital defects (UTCD) with other congenital malformations in a group of children registered in the Polish Registry of Congenital Malformations (PRCM) in the Pomeranian district from 1999 to 2001.

Material and methods: Among the 70721 live births during this period the 1070 (1.65%) children with congenital malformations were registered in the PRCM. Among them 126 children (57 girls and 71 boys) had UTCD, which was 13% of all recognized malformations.

Results: The prevalence of UTCD in our population was 1.58 per 1,000 births; which is medium. We found 70 cases (55.6%) of sole abnormality of the urinary tract, while in the 56 cases malformations were more complex. In 50
children (39.7%) the coexistence of UTCD with other congenital anomalies was observed, including cardiovascular in 16.7%, musculoskeletal in 15.9%, central nervous system in 11.9%, gastrointestinal in 9.5% and genital in 6.4% children. In 20 children (15.8%) multiple congenital anomalies have been recognized. These occurred frequently with uni- (n=5) and bilateral (n=4) kidney agenesis and polycystic kidney (n=4). Chromosomal abnormalities were found in four cases (21 trisomy in three cases and ring 18 in one). Moreover, in three children the VATER association phenotype was observed. One case of Ehlers-Danlos and one case of Cornelia de Lange syndrome were diagnosed.

Conclusions: UTCD coexist with other congenital anomalies, especially cardiovascular and musculoskeletal with high incidence. For these reasons, routine examination for other systems should be mandatory in children with urinary tract congenital defects.

(P 25)
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ASSOCIATED MALFORMATIONS AND CHROMOSOMAL DEFECTS IN CONGENITAL DIAPHRAGMATIC HERNIA
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Objectives: The authors of this study reviewed the records of all neonates with congenital diaphragmatic hernia (CDH) in order to determine the frequency and nature of malformations and chromosome abnormalities associated with CDH.

Material and Methods: We performed a retrospective study of 55 newborns with CDH referred to the Institute of Polish Mothers Memorial Hospital (Neonatal Intensive Care Unit) over a last decade period (1992-2002). The study population was divided into two groups. The first group consisted of 36 (65%) newborns who died during hospitalization. The second one was composed of 19 (35%) survivors.

Results: In total, 17 of 55 infants (31%) with CDH had additional anomalies. Most frequent (in 7 patients) there were congenital heart defects (hypoplastic heart syndrome, atrial and ventricular septal defect, Fallot syndrome, coarctation of aorta) and urinary tract anomalies (hypospadias and vesicoureteral reflux in 6 patients). Furthermore following associated malformations occurred in the study population: skeletal anomalies (6), cleft palate and lip (2), meningomyelocele and hydrocephalus (2), encephalocele (1), omphalocele (1) and abnormal facial profile (3). In 2 of patients chromosomal abnormalities were found (trisomy 18, aberration). Incidence of familial CDH was reported in 3 patients.

Subgroup analysis showed that occurrence of associated malformations was significantly higher in first group of patients comparing to survivors (31% vs. 15%).

Conclusion: Associated anomalies occur frequently in patients with CDH with incidence of 17%. Occurrence of additional malformations and chromosomal abnormalities is associated with poor prognosis in neonates with congenital diaphragmatic hernia.

(P 26)
P Krajewski, P Sieroszewski, K Jarosik, M Pokrzywnicka, E Welfel
EPIDEMIOLOGY OF CONGENITAL MALFORMATIONS AMONG NEWBORNS BORN ALIVE IN THE INSTITUTE OF GYNECOLOGY AND OBSTETRICS IN LODZ IN THE YEARS 2000-2003
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Purpose: In the Łódź region IG&O MU was one of the first institutions that joined the program called PRWWR and took part in its dissemination. The aim of our work was to evaluate the frequency of occurrence of congenital malformations among newborns born alive in IG&O MU in Łódź in the years 2000-2003 in comparison with the data from the whole Łódź region acquired after the implementation of the system registering all malformations in PRWWR.

Material: The research included all newborns born alive in the Institute of Gynecology and Obstetrics, Medical University of Lodz during the period analyzed. The data was acquired from the newborns’ case records as well as other medical documentation. The results were compared with the demographical analysis of the Łódź region.

Results: Among 113706 newborns that were born alive in the region of Łódź 7881 were born in IG&O MU in Łódź; including 184 (2.33%) with congenital malformations. During the period analyzed (4 years) 1292 newborns were registered in PRWWR as having diagnosed inborn developmental anomalies, including 14,24% (that is 184) that were born in IG&O MU. The malformations occurring most frequently in the period analyzed were congenital heart diseases and malformations of the circulatory system Q 20-28 – they occurred in 361 cases. The number includes 42 cases registered from IG&O MU (11.63%). The second most frequent were malformations and defects of the muscular-skeletal system Q 65-79 – they occurred in 243 cases in the region, including 41 cases (16.87%) diagnosed in IG&O MU. The third most often were malformations of the urinary-sexual organs Q 50-64 – they occurred in 223 cases
including 37 cases (16.59%) from IG&O MU.

In the Łódź region the birth rate during the years analyzed was negative (below 0) and it was on the level of -3.2 to -3.6 ‰. Newborns morbidity equaled from 6.9 to 8.8‰. Among 848 deaths of newborns in the perinatal period in the region of Łódź 235 (27.71%) were caused by inborn developmental anomalies.

Discussion: Congenital malformations are still one of the most significant problems of contemporary neonatology. They are also listed among the main reasons of deaths in case of fetuses and newborns. The Polish Central Register of Inborn Developmental Anomalies is the register that enables us to solve the problem of malformations in the whole country. The frequency of occurrence of congenital malformations remains on a stable level.

Conclusion:
1. Inborn developmental anomalies are still one of the main reasons causing deaths among newborns in the perinatal period.
2. Introducing PRWWR enables a deep analysis of epidemiology of occurrence regarding inborn developmental anomalies in the region examined.
3. The most frequent malformations occurring in the region of Łódź, and also diagnosed in IG&O MU, are the malformations of the circulatory system as well as malformations of sexual organs and the skeletal system.

(P 27)

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The authors present the results of a retrospective analysis of incidence and type of congenital defects in newborns born at the Department of Neonatology Center of Medical Postgraduate Education in the years 1999-2001 and 2003-2004. We analyzed the influence of prenatal diagnosis on neonatal mortality caused by congenital defects in the first month of life.

In this study 585 (9%) cases of congenital malformations were detected in the group of 6495 live births. The most common in this group were: urogenital systems defects (28%), neural tube defects (23.9%) and cardiovascular system defects (13.7%). We have observed the increasing incidence of congenital malformations with simultaneous improved survival in this group of children.

In about 70% of cases the diagnosis was made prenatally, what allowed planning and the appropriate way of delivery and management of the neonate.

The collaboration between specialists of prenatal medicine, neonatologists, surgeons, etc, improves the survival rate and allows normal development of those children.

(P 28)

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The development of sexual organs is of several stages. The disorder of this process influences either the clinical distinct features of the process of gonad differentiation or generation malformations of sexual organs.

The objective of this study is to evaluate the frequency and type of sexual organs malformations in newborns hospitalized in the Neonatal Intensive Care Unit in Bydgoszcz. Congenital malformations were recognized in 645 among 10412 (6.19%) newborns born between 2000-2004. The congenital malformations of external sexual organs were recognized in 51 newborns which constitutes 7.9% of all newborns with malformations and 0.48% of all newborns. In 16 cases the malformations occurred within a group of malformations. Turner's; 46,XX,inv(Xp), 45,X, was recognized twice, Patau syndrome 46,XY,der(13;14),+13, was recognized ones, Prader-Willi syndrome was recognized ones.

The most frequent malformation of external sexual organs was hypospadias and cryptorchidism, which was recognized in 39 newborns. In 15 cases coexistence of other malformations was recognized. The malformations of external sexual organs constituted almost 8% of all malformations. Hypospadias and cryptorchidism constituted ¾ of external sexual organs malformations.

In every third patient with recognized hypospadias and cryptorchidism other malformations can be expected.
(P 29)
Z Murowaniecki, A Buczyńska, S Tarkowski
SPATIAL EVALUATION OF BIRTH DEFECTS AND ENVIRONMENTAL HAZARDS IN POLAND - PILOT STUDY
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Introduction: A subarea from the Polish Registry of Congenital Malformations (subPRCM) in the west north Poland was selected for the study.
The aim of study was to evaluate differences in spatial distribution of birth defects incidence rates within the subPRCM, identification of locations with the highest rates and description of environmental hazard profiles of these clusters.

Methods: Spatial autocorrelation of the birth defect cases was tested. The birth defect cases were aggregated to communes with respect to all defects and specific groups (according to ICD10). One-side Fisher's exact test was applied to identify communes with the index significantly statistically greater than the mean for the whole subPRCM.
The environmental hazards indexes for air pollution, accumulated solid wastes, untreated sewage and percentage of population supplied chlorinated drinking water have been also aggregated to the integrated index of environmental health hazard.

The index of birth defects incidence was significantly higher in 47 communes in 1998, in 36 communes in 1999 and in 27 communes in 1998 and in 1999 combined, than the mean value for the whole subPRCM.

Discussion: Spatial analysis of the distribution of birth defects indicated that there are cluster areas where the incidence of birth defects is significantly higher than the average for all cases.
In view of limited environmental data it was not possible in this pilot study to assess correlation between incidence of birth defects and indexes of environmental hazards.

(P 30)
M Baumert, E Rokicka-Bulandra, M Paprotny
CARDIOVASCULAR MALFORMATION IN NEWBORN FROM NEONATOLOGICAL DEPARTMENT OF SILESIAN MEDICAL SCHOOL
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Etiology:

(P 31)
M Constantinou, Z Helszer, B Kałużewski
THE CLINICAL APPLICATIONS OF THE MOLECULAR CYTOGENETICS TECHNIQUES IN SELECTED CHROMOSOME ABERRATIONS
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Molecular cytogenetics (FISH technique) has essentially improved the diagnostic of genetically determined diseases, raising the diagnostic potential to a new level. The new diagnostic tools of molecular cytogenetics allow – at present – for detection of rare subchromosomal rearrangements, such as microdeletions or chromosomal duplications in cases of congenital malformation syndromes and/or mental retardation.
The role of the FISH technique (Fluorescence In Situ Hybridization) has well been documented, while the application of CGH (Comparative Genomic Hybridization) or mCGH (microarray-CGH) techniques remains still a controversial issue. Therefore, it is particularly important to determine the position of molecular cytogenetics in cytogenetic diagnostics, so that the results of the tests were reliable and interpreted by the clinician in an unequivocal way. In the presented study, it was attempted to define localisation of the above mentioned techniques in clinical environment on the basis of application of FISH, M-FISH and CGH techniques in selected cases of chromosome aberrations.
Deletion within the chromosome region of 22q11 may occur in patients with three syndromes: DiGeorge (DGS-mutation is present in 83-88% of patients), velocardiofacial (VCFS or Shprintzen syndrome-mutation is present in 68-81% of patients) and conotruncal anomaly face syndrome (CTAFS or Takao syndrome-mutation is present in 84% of patients).

22q11.2 microdeletion syndrome affects 1/4000 births. Inheritance is autosomal dominant. Del(22)(q11) is present in 5% of all newborns with cardiac defects and in 10-29% of those with isolated conotruncal cardiac defects. In 12% of cases, also one of the parents, not suspected earlier to be affected by this abnormality, has del 22q11.2.

The aim of the study was to evaluate incidence of 22q11.2 microdeletion in children with congenital conotruncal cardiac defects and at least one typical feature of this microdeletion syndrome, in parents of children who died because of congenital cardiac defects, and in parents of children with microdeletion 22q11.2.

109 patients have been examined till now: 63 children with cardiac defect (all born 1996-2005), 30 - parents of children who died because of cardiac defects, 16 - parents of children with microdeletion 22q11.2.

In all patients both routine cytogenetic examination (at least 550 band resolution) and FISH technique using TULPE1 probe was used.

Microdeletion 22q11.2 was detected in 14 out of 63 examined children (22.22% of affected children). Among 14 children with microdeletion, in 13 children DGS, and in one child VCFS features were present. Among parents of 8 affected children, in one case mutation was inherited from a “healthy” father. No cases of microdeletion 22q11.2 were detected among the dead children.

We confirm other authors’ observations that the search for microdeletion 22q11.2 should be performed in the cases of conotruncal cardiac defects and at least one typical feature of this microdeletion syndrome.

Williams-Beuren syndrome (WBS; OMIM #194050) is a complex developmental disorder occurring in 1:20000, characterised by distinctive facial dysmorphism, cardiovascular abnormalities, growth delay, mental retardation, unusual behavioral profile and infantile hypercalcemia.

The aim of the presented study was to estimate the spectrum of features in patients with the diagnosis of WBS confirmed by FISH analysis, who were registered in our centre with the clinical suspicion of this syndrome. The thorough clinical, anthropometric and cytogenetical evaluation has been made for 44 individuals. The study of the cohort enabled us to outline the most common dysmorphic features and congenital defects as well as usual developmental pattern of affected individuals. Our findings are also discussed in the view of current scientific reports.

Because WBS at the early age is not easy to recognise, we present some clues to make the proper diagnosis more prompt. All our patients with the typical WBS phenotype were hemizygotic for the ELN locus. However, along with the recognition of characteristic dysmorphic features, in each case we find the performance of FISH analysis to be an indispensable part of the clinical investigation leading to the final diagnosis of WBS.
Noonan syndrome (NS, OMIM 163950) is an autosomal dominant genetic disorder characterized by the following clinical symptoms: short stature, congenital heart defects, pectus deformities, pterygium colli, mild mental retardation and facial dysmorphism: hypertelorism, epicantic folds, low-set, prominent ears. Recently discovered PTPN11 mutations (gene located on the 12th chromosome p24.1) are responsible for NS in almost half of the cases. The following inclusion criteria for molecular testing were used: dysmorphic features, short stature, congenital heart defects, pectus deformities or pterygium colli and cryptorchidism. Detailed clinical evaluation, including family history, dysmorphic features, pre- and postnatal development and congenital malformations, was performed.

The most frequent symptoms in our group of patients were: dysmorphic features (hypertelorism (100%), low-set ears (79%), short neck (93%)), congenital heart defects (93%), short stature (79%) and pectus malformations (57%). To determine the character of mutation in the PTPN11 gene, we performed a direct sequencing analysis of the exons 2-15. Mutation in PTPN11 gene was identified in 4 of 15 investigated patients. One mutation c.846C>G in exon 7 is novel; two others were previously reported – c.188A>G (exon 3) and c.1510A>G (mutation inherited from mother). All patients with PTPN11 mutation demonstrated typical symptoms of NS, such as: short stature, congenital heart defects, widened nipples, pterygium colli and thick ear helix. The pulmonary stenosis (typical for NS) was found only in one patient, whereas the other three had different types of cardiac malformations.

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DU PAN SYNDROME PHENOTYPE CAUSED BY HETEROZYGOUS PATHOGENIC MUTATIONS IN CDMP1 GENE
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Du Pan syndrome is a rare acromesomelic dysplasia with characteristic clinical and radiographic findings. It is inherited as an autosomal recessive trait. Almost all the patients reported have been from Muslim countries. We report a female and her child with Du Pan syndrome from a Caucasian, Polish family. Three new heterozygous mutations clustered on one allele of the CDMP1 gene were identified in the affected individuals resulting in the first familial case with dominant Du Pan syndrome. A possible dominant negative effect of the alterations - located in the active domain of the mature CDMP1 protein - is likely to be responsible for the clinical expression of the disorder.

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A NOVEL MUTATION IN IRF6 CAUSES VAN DER WOUDE SYNDROME
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Van der Woude syndrome (VWS, OMIM 119300) is the most common type of syndromic orofacial clefting characterised by pits of the lower lip, hypodontia and cleft lip and/or cleft palate. It is inherited in an autosomal dominant way and exhibits very high penetrance with varied expressivity. The prevalence of VWS varies from 1:10,000 to 1:40,000 still born or live births. Van der Woude syndrome has been associated with mutations localised in the interferon regulatory factor 6 gene (IRF6). Protein product of this gene belongs to a family of nine transcription factors that share a highly conserved DNA binding domain and less well-conserved protein binding domain. The function of the normal gene product is still unknown.

The aim of the study was to search for mutations of IRF6 in two families affected with Van der Woude syndrome in an attempt to explain the reason of this craniofacial disorder. Peripheral blood samples were collected from affected and unaffected family members and 150 healthy individuals (controls). Genomic DNA was isolated by salt extraction and the entire coding sequence comprising exons 3 to 10 was PCR-amplified with the use of designed primers. Multi-temperature single stranded conformational polymorphism analysis (MSSCP) of IRF6 showed an abnormal mobility of a single stranded DNA fragment of exon 7 in two affected individuals from the same family. Direct sequencing revealed a novel heterozygous mutation 931insT that has not been detected in any of the unaffected family members as well as in 150 controls. This novel insertion, which results in a frasmeshift and premature termination of translation at 337 amino acid residue, is localised in the conserved region
encoding protein binding SMIR domain.

Our results support the view that mutations in IRF6 constitute a major causative factor of Van der Woude syndrome. The novel insertion might be responsible for this developmental malformation, since it might disturb the regulatory function of the encoded protein and result in an abnormal fusion of nasal and maxillary processes during embryogenesis. Supported by grant no. P04 A 092 26

(P 37)
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IDENTIFICATION OF NOVEL MUTATIONS AND A NEW POLYMORPHISM IN THE TCOF1 GENE IN THE PATIENTS WITH TREACHER COLLINS SYNDROME

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Treacher Collins syndrome (TCS) [OMIM 154500], the most common type of mandibulofacial dysostosis (MFD), results from malformation of the structures developing from the first and the second pharyngeal arches during early embryogenesis. TCS is inherited in an autosomal dominant fashion and the estimated incidence is 1 in 50,000 live births. The major features of the disease include midface hypoplasia, micrognathia, microtia, conductive hearing loss and cleft palate. It is believed that mutations of TCOF1 gene are responsible for the symptoms of TCS. So far, 112 TCOF1 different mutations have been described in 155 unrelated patients, mostly resulting in a truncated protein product of the gene.

We investigated the structure of TCOF1 in 58 patients with TCS and their 42 relatives. The DNA fragments were amplified by PCR and subsequently were subjected to SSCP and MSSCP analysis followed by direct sequencing. In the group of patients with TCS was identified five novel mutations: c.376_378+15delAAGGTGAGTGGGACTGCC in exon 4, c.484_668ins185bp in exon 5, c.2373_2374delAG and c.2344C>T in exon 15, c.3880G>T in exon 23 and one mutation c.786_787delAG in exon 7, described in literature. The mutations of one of the TCOF1 alleles may cause TCS by haploinsufficiency of treacle, resulting in an abnormal craniofacial development. Moreover, were detected: one novel polymorphism c.2428_24delCTCTC in intron 15 and four previously described polymorphisms: c.639+32C>T in intron 6, c.1347C>T in exon 10, c.2429 T>C in exon 16 and c.3938 T>C in exon 23. The detected polymorphisms, however, showed no correlation with the occurrence of the TCS symptoms. Amplification of the fragments harbouring deletions using LightCycler showed that alleles harbouring mutations exhibit a second melting temperature peak, different from that of the normal allele. It was suggested that this method might be used in screening for the mutations in the TCOF1.

Our results indicate the importance of molecular diagnostics in Treacher Collins syndrome for prenatal and postnatal screening and genetic counselling.

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(P 38)
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ANALYSIS OF THE MTHFR POLYMORPHISMS AS RISK FACTORS OF NEURAL TUBE DEFECTS IN POLAND

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Background: Neural tube defects (NTDs) have been associated with common polymorphisms of the methylenetetrahydrofolate reductase (MTHFR) as well as with biochemical factors involved in the conversion of homocysteine to methionine.

Methods: The prevalence of the C667T and A1298C MTHFR polymorphisms among 69 NTD affected cases and their parents (69 children, 83 mothers, 76 fathers) and 267 healthy controls was investigated. The study group was recruited through the Association for Spina Bifida of Poland, the control population was obtained from the patients of primary health centre and pregnant women attending maternity clinic in Warsaw. Both populations fulfilled criteria of Hardy-Weinberg equilibrium.

Results: Observed frequencies of the 667TT genotype were 10,1% in NTD children, 8,4% in mothers, 7,9% in fathers and 8,6% in control group. 7,9% of NTD children, 6,0% of mothers, 11,9% of fathers and 7,9% of controls were the carriers of the 1298CC genotype. Comparison of genotype frequencies between NTD triads and control groups did not reveal statistically significant difference for either of the polymorphism analysed. The approximate allele frequencies were 0,67 and 0,33 for C and T alleles in the C677T polymorphism and 0,67 and 0,33 for A and C alleles in the A1298C polymorphism respectively.
The transmission disequilibrium test was performed on 68 child-parents triads. This analysis showed preferential transmission of a 677T/1298A haplotype among doubly heterozygous parents (transmitted : nontransmitted – 41:23, but the analysis failed to reach statistical significance (p=0.08)). The MTHFR genotype combinations 677CT/1298CC, TT/AC, and TT/CC were not observed. All individuals homozygous for one MTHFR mutation were homozygous wild-type for the other. Conclusions: In the sample of Polish population studied no statistically significant association between MTHFR polymorphisms and greater risk of having an offspring with NTD has been found. However parental preferential transmission of a 677T/1298A haplotype to a children with NTD needs further investigation.

(P 39)
M Berner-Trąbska, M Perenc, K Jędrychowska-Dańska, E Kasprzak
ANALYSIS OF POLYMORPHISM C677T MTHFR GENE IN THE CASES OF OPEN NEURAL TUBE DEFECT: PRELIMINARY REPORT
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Aim: The aim of this study was to examine one of many possible factors conditioning formation of the defects of the neural tube (NTD) as well as to test of a group of female patients exacting substitutes of the folic acid in the period of preprocreation.

Material and methods: The investigations were conducted in a group of neonates with open NTD, their parents as well as in the control group. The analysis of polymorphism C677T gene encoding 5.10-methylenetetrahydrofolate reductase was performed (MTHFR) and homocysteine concentration was marked.

Results: Frequency of C allele in the group of neonates with NTD amounted to 0.57, however, T allele to 0.43. Among the parents of the ill children these frequencies were 0.63 for C allele and 0.38 for T allele, respectively. In the reference group C allele frequency was 0.68 but T allele 0.32. The concentration of homocysteine both in the control and the studied group were slightly higher in subjects with the CT genotype in comparison to subjects with CC genotype.

Discussion: The frequencies of alleles obtained in the control group are convergent with frequencies published by other investigators. In the control group the frequency of C allele was 0.68 compared with 0.64 in British population [Papapetrou] and 0.69 in German population [Koch]. However, the frequency of T allele was 0.32 compared with 0.36 in British population [Papapetrou] and to 0.31 in German population [Koch]. In group of children with NTD the frequency of C allele was lower (0.57) in comparison with British population (0.63) [Papapetrou] and with German population (0,66) [Koch], however, the frequency of T allele (0.43) was higher in comparison to British (0.37) [Papapetrou] and German population (0.36) [Koch].


Conclusions:
1) The frequency T allele in position 677 of the gene of 5,10-methylenetetrahydrofolate reductase is higher in the group of the parents and neonates with open NTD than in the control group.
2) Mean homocysteine concentration is higher in patients with CT genotype (in the control group, parents and neonates with NTD) as compared with patients with the CC genotype.

(P 40)
E Hand
SOCIO-ECONOMIC DEPRIVATION AND PREGNANCY OUTCOME IN NORTHERN IRELAND
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Aim: This study set out to investigate the effect of socio-economic deprivation on pregnancy outcome in Northern Ireland, with particular respect to congenital anomalies.

Method: Data were available from the Registrar Generals Office for the period 1991 to 2002, in the form of stillbirths, infant deaths and live births. For the time period of the study there were 161 stillbirths due to congenital anomalies and 661 infants deaths due to congenital anomaly. For the purposes of analysing the data, the following subgroups of congenital anomalies were formed: chromosomal anomalies, non-chromosomal anomalies, heart defects and central nervous system defects.

As there is an 11 year time period in the study, trends in any of the mentioned groups was of interest as well as an association with socio-economic deprivation. The Noble index for income deprivation was used as a deprivation
indicator. Poisson regression analysis was used to determine any trending over time or deprivation quintiles, and it was also used to determine if there was interaction between time and deprivation level.

Results: There was no trend over time in the occurrence of congenital anomalies among stillbirths and early infant deaths (SBID), however there was a trend across deprivation levels, with those in more deprived quintiles being more likely to have a SBID due to congenital anomalies. Central nervous system disorders increased (p=0.006), with increasing deprivation, among SBID, however there was no decrease over time. Heart defects showed a substantially linear decrease over time (p=0.006) across all deprivation levels. There was strong interaction between time and deprivation level for SBID due to non-chromosomal anomalies, with SBID increasing over time for the less deprived and decreasing over time for the more deprived.

Conclusion: The extended perinatal mortality (EPM) was calculated and compared with similar figures obtained for England and Wales, surprisingly the incidence ratio for Northern Ireland was higher than that for England and Wales for chromosomal anomalies, non chromosomal anomalies, neural tube defects and cardiac defects.

(P 41)
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CYCLOOXYGENASE INHIBITORS INCREASE THE RISK OF THE HEART VENTRICULAR SEPTAL DEFECTS
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Ventricular septal defects are common congenital abnormalities. They are associated with maternal age and various environmental factors. The aim of the study was to evaluate the effect of prenatal exposure to cyclooxygenase (COX) inhibitors on the heart defects in rats. A retrospective statistical analysis was performed using data collected in our laboratory during various teratological studies, in the years 1997-2004. The observations were compared with concurrent and historic control data, as well as findings from other developmental toxicological studies with selective and non-selective COX-2 inhibitors. In spite of insignificant differences in the occurrence of the ventricular septal defects between drug-exposed and the corresponding control groups, the summary statistical analysis done using the Mantel-Haenszel (two-sided) test and historical control data revealed higher incidence of the heart malformations in offsprings exposed to COX-inhibitors. Unlike other specific inhibitors, aspirin and ibuprofen significantly increase the occurrence of cardiac septal anomalies. It could be concluded that prenatal exposure to COX-inhibitors, especially aspirin and ibuprofen, increased the occurrence of the ventricular septal defects in rat’s offsprings.

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(P 42)
K Mazur-Melewska, W Służewski
RUBELLA VIRUS AS THE ENVIRONMENTAL PATHOGEN CAUSING CONGENITAL DEFECTS IN FETUS AND DEVELOPMENTAL ABNORMALITIES IN INFANTS.
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Rubella virus is one of the best known environmental causes of congenital defects in fetus. It is also the pathogen which can be radically eliminated. In spite of the vaccinations, sporadic cases of congenital rubella are still registered. The aim of this study was to evaluate clinical manifestation of children with congenital rubella infection in the long follow-up analysis.

Material and methods: We prospectively analyzed 10 children (6 girls and 4 boys), born between 1992 and 2000, whose mothers suffered from symptomatic rubella between 5th and 13th week of pregnancy. The infants’ infection was confirmed by serological tests. The follow-up observation was performed for 24 months.

Results: Congenital malformations were found in all children. The most frequent were congenital heart defects (9 cases), with ASD (7 cases) and PDA (3 cases). The heart defects were either isolated or combined. Next most frequent were abnormalities of head’s bones with enlarged anterior fontanel (more than 3 x 3 cm in the first month of life). Congenital microcephalus was diagnosed in 4 infants. Congenital cataract of both eyes was found in 1 case. The active inflammation in internal organs enhanced the abnormalities caused by rubella virus in the first months of life. Among others we observed: interstitial pneumonia (4 cases), encephalitis (2 children), myocarditis (1 child) and chronic ileitis (2 children). In the two-year follow-up we found more developmental abnormalities closely connected with congenital rubella. In 9 children we observed hearing deficit, which was diagnosed as total deafness in 2 cases. The neurodevelopmental milestones were delayed in 5 children. Postnatal microsomia was found in 4 children.
Conclusion: In spite of the open vaccination program, rubella virus is still a significant environmental factor causing congenital defects in fetus and increasing complications in the postnatal period.

(P 43)
K Mazur-Melewska, W Służeński
ANTIRETROVIRAL TREATMENT DURING PREGNANCY OF HIV-POSITIVE WOMEN AS A ENVIRONMENTAL FACTOR OF CONGENITAL DEFECTS IN THEIR CHILDREN.
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The number of women in Poland infected by HIV increases every year. Most of them are in the reproductive age. The prophylactic with the beginning or continuation of the antiviral treatment during pregnancy radically decreases the risk to give birth to an HIV-infected child. Application of new antiretroviral treatment poses a question about its possibility to cause congenital defects.

The aim of study was to evaluate the effect of antiretroviral treatment during pregnancy, delivery and the first 6 weeks of life on the incidence and type of congenital defects found in HIV-positive mothers’ children.

MATERIAL AND METHODS: We performed a prospective study of 16 infants (9 girls and 7 boys) born by HIV-positive mothers, who had received the antiviral treatment (mono or politherapy) during pregnancy and delivery. The children were born between 1997 and 2005. The studies were conducted during min. 5 months in order to define the serological status. At the enrolment children underwent detailed evaluation, including clinical assessment, ultrasonography and electrocardiograph. The X-rays were done only in some necessary situations.

RESULTS: Four children were diagnosed as having the congenital defects. There were: fused kidneys – 1 case, hydrocele – 1; heart defect: trace FoA – 1; cranium malformation – additional bones in the lambdoid suture – 1). We did not observe domination of any organ or system in the congenital defects. None of them produced the medical intervention

CONCLUSION: The documented advantage of the antiretroviral therapy during pregnancy, which reduced the risk of infection from 30 to nearly 2 percent, predominated over the possibility to stimulate congenital defects in infants.

(P 44)
E Kasprzak, K Kocemba, B Stońska, J Wilczyński, J Gadziniowski
LOW AND HIGH RISK FACTORS IN NEONATES WITH CONGENITAL CYSTIC ADENOMATOID MALFORMATION OF LUNGS (CCAM) TREATED IN POLISH MOTHERS MEMORIAL HOSPITAL RESEARCH INSTITUTE (1991-2005).
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Introduction: Congenital cystic adenomatoid malformation of lungs (CCAM) is a rare congenital malformation of the respiratory system with unclear etiology. In literature, among different harmful genetic factors, mother's illnesses, uterus' illnesses, pathology of placenta and viral infections during pregnancy are usually emphasized. The aim of the work was to establish low and high risk factors in particular CCAM types based on the history date in the reference centre. Material and methods: We assessed 27 neonates with different types of CCAM (type I, II, III), which were diagnosed and/or treated in the Department of Neonatology of PMMHRI in 01.01.1991 - 31.03.2005. 8 cases of CCAM type I (29.7%), 10 cases of CCAM type II (37%) and 9 cases of CCAM type III (33.3%) have been recorded. Diagnostic criteria for low and high risk pregnancies were established based on the history. Low risk pregnancies (LRP) were defined as a pregnancies in young (18-34 years old), healthy women with no history of serious diseases, no drug use or any problems during pregnancy. High risk pregnancies (HRP) were defined as pregnancies in women over 35 years or age, or under 17 years, with family history regarding congenital malformations and/or chromosome aberrations, spontaneous abortion, intrauterine death, congenital malformations in previous pregnancies, mother's illnesses (diabetes, epilepsy, cholestasis, circulatory system illnesses, thyroid gland problems and connective tissue illnesses), in vitro fertilization and serologic incompatibility. Results: In the group of 27 pregnant women who delivered neonates with different types of CCAM, 14 neonates were from LRP (14/27 – 51.8%) and 13 from HRP (13/27 – 48.2%). In CCAM type I most cases were LRP (5/8 – 62.5%). In CCAM type I most cases were LRP (5/8 – 62.5%). In the group with CCAM type II 7 out of 10 cases were HRP (70.0%). In the group of neonates with CCAM type III most cases were from LRP (6/9 – 66.6%). Conclusions: 1. Most pregnancies of low risk factors were noted in the group with lethal type of CCAM (type III – 66.6%). 2. There were no statistically significant differences in the presence of low and high risk pregnancies between particular types of CCAM (Fisher's test p > 0.05). 3. The most frequent risk factors were mother's illness, mother's age over 35 years, and previous spontaneous abortions.
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TOCOPHEROL LEVELS IN MOTHERS OF CHILDREN WITH CLEFT LIP OR WITH CLEFT LIP AND PALATE

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Objectives: Analysis of environmental risk factors should be performed separately for non-syndromic cleft lip (CL) and cleft lip and palate (CLP) because CLP is not the same as CL. Isolated CL forms during the first weeks of embryonic development when metabolism is essentially anaerobic, antioxidant enzymes are not developed, and hypothetical deficiency of \(-\)tocopherol (\(\alpha\)-T) may be crucial.

Aim: The goal of the study was to investigate concentrations of \(\alpha\)-T in women who gave birth to a child with isolated cleft lip and mothers of children with cleft lip and palate.

Material and methods: Blood samples from 31 healthy mothers of children with isolated CL and 29 healthy mothers of children with isolated CLP were collected. Fasting plasma \(\alpha\)-T concentrations were measured by the HPLC. Kolmologorov-Smirnov test with Lilefors correction and k-means cluster analysis were applied to determine differences between the groups of women.

Results: We found that \(\alpha\)-T concentrations were lower in CL compared to CLP, but the difference did not achieve the level of statistical significance (medians: 15.8\(\mu\)mol/L vs. 20.0\(\mu\)mol/L; \(p=0.066\)). Three clusters of \(\alpha\)-T concentrations were identified: 14.0\(\mu\)mol/L (19CL+8CLP), 19.6\(\mu\)mol/L (8CL+13CLP), and 21.1\(\mu\)mol/L (4CL+8CLP). The distribution of results to the clusters depended on the type of orofacial cleft (chi squared=6.95, d.f.=2, \(p=0.031\)).

Conclusions: The heterogeneity of plasma vitamin E status in mothers of children with cleft lip with or without cleft palate was demonstrated. The role of periconceptional intake of antioxidants in reduction of risk of giving birth to a child with orofacial cleft requires further research.

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THE ROLE OF INTRAUTERINE LACK OF SPACE IN MULTIPLE PREGNANCY FOR THE DEVELOPMENT OF THE HIP

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In this prospective study the role of lack of space in twin pregnancy for the development of hip was analysed using ultrasonography. In Poland, the prevalence of de velopmental dysplasia of the hip (DDH) is 6.5\%. The etiology of DDH is multifactorial and is influenced by mechanical, hormonal and genetic elements. Several predisposing factors have been identified (ligamentous laxity, prenatal and postnatal positioning, racial predilection). It is well documented, that breech position in singleton pregnancies is associated with DDH. The aim of this study was to: 1. Estimate the incidence of DDH in examined twins. 2. Estimate the influence of intrauterus lack of space associated with twin pregnancy for the development of the hip. 3. Analyse the role of DDH risk factors.

4. Analyse correlation between infertility treatment and incidence of DDH. For this purpose 80 hip joints of 40 newborn twins were examined every 6 weeks clinically and ultrasonographically (Graf method, FHC method) till the age of 6 months. We compared the values of the alpha and beta angle related to different position in uterus, birthweight, gender, length of gestation, positive family history and infertility treatment. In the group of 40 twins we found the type Ia+ in one left hip (1.25\%). The rest of the hip joints were classified as type Ia and Ib according to Graf. The value of FHC was bigger than 50\% in all cases, and had tendency to increase in successive examinations. None of twins required treatment. We found 40\% (16/40) breech presentations at birth in the entire group. Positive family history of DDH was present in 5\% (2/40). Positive family history of twins was present in 37.5\% (15/40). In the group of multiples, whose parents had gone infertility treatment, the initial values of beta angle was higher.

It seems, that twin pregnancy cannot be regarded as a risk factor for DDH. We suppose also, that breech presentation in twin pregnancy is not a risk factor for DDH. It seems, that the biggest remodeling of the hip joints occurs between 6 and 12 weeks of age.

Prevention and prenatal diagnosis:

(\(P\) 47)

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ADOLESCENTS KNOWLEDGE ABOUT FOLIC ACID AND ITS IMPORTANCE IN PREGNANCY- A SURVEY
Problem: In pregnancy the avoidance of addictive drugs, smoking and alcohol and the knowledge about the role of folic acid is very important. In the medical and laymen journalism the periconceptional supplementation of folic acid is widely recommended because of the prevention of congenital malformations, e.g. neural tube defects. We know that only 7% of pregnant women in Saxony-Anhalt take in folic acid in the period at least 4 weeks before conception and 3 month of the pregnancy. The aim is to give information about general behaviour before and in pregnancy in time. A good moment could be biology in school.

Methods: We performed a representative interview from March to June 2004. We posted standardized questionnaires about folic acid and its importance in pregnancy to adolescents of 15 secondary and 18 comprehensive secondary schools in Saxony-Anhalt.

Results: A total of 4332 adolescents aged from 15 to 21 years answered the questionnaires, about 2632 girls (61%) and 1685 boys (39%). 62% of all interviewed persons took notice of the term “folic acid”, but only 5% knew that is a vitamin. A very small share of adolescents knew the function of folic acid in generally. Also less adolescents knew special foods containing folic acid and importance of folic acid. Only 22% of adolescents answered that folic acid should be taken before and in pregnancy. Whereas nearly all interviewed persons knew the provisions in pregnancy, e.g. “no smoking” and “no alcohol”.

Conclusions: Our survey shows that the level of awareness about folic acid in schools is very low. We suggest the general acceptance of the problem “folic acid and pregnancy” in the course of instruction in the biology in school. Because the adolescents of today will be the parents of tomorrow!

Folic acid supplementation during periconceptional period reduces risk of neural tube defect in offspring by 70%. Prevalence of neural tube defects (NTD) in Wielkopolska region equalled 10,83 per 10000 live and still births in 2002 as assessed by EUROCAT database, and is much higher than in many European countries.

The National Primary Prevention Program of Neural Tube Defects started in 1997 in Poland at the Department of Epidemiology of the National Institute of Mother and Child in Warsaw. Surveys on knowledge, attitudes and behaviours toward folic acid were conducted among women aged 20-34 years in 5 chosen administrative regions - voivodships in 2001 (n=671) and 2003 (n=649) as tools for the evaluation of the effectiveness of the program. The samples were taken from patients of the primary health centres in 31 randomly selected administrative subregions in every voivodship, proportionally to number of residents and urbanization rate. There were 115 in 2001 and 93 in 2003 pregnant women in the study sample.

The proportion of pregnant women taking folic acid during the pregnancy increased from 46% in 2001 to 76% in 2003, before the pregnancy – from 14% to 17%, and 4 weeks or more before the pregnancy – from 12% to 13% respectively. The proportion of non-pregnant women taking folic acid in recommended dose at least 0,4 mg daily decreased from 15% in 2001 to 12% in 2003, what was accompanied by the decrease of intake of any vitamin supplements from 57% in 2001 to 51% in 2003. The only subgroups of non-pregnant women in which decrease in intake of folic acid in recommended dosage was not noticed between the two periods were women aged 25-29 years (17% in 2001 and 17% in 2003), students and women with academic degree (19% in 2001 and 20% in 2003) and women planning to be pregnant in the future (15% in 2001 and 15% in 2003).

The improvement in the level of knowledge on folic acid in Polish women was noticed between 2001 and 2003 as well. The proportion of women knowing that folic acid is beneficial for fetal development increased from 23% in 2001 to 35% in 2003 and the proportion of women knowing that folic acid supplementation should begin before the pregnancy, increased from 22% in 2001 to 30% in 2003. The increase of knowledge on folic acid noticed between 2001 and 2003 was independent on age, socio-economic status and pregnancy status.
Aim: The aim of the study was to analyse the clinical courses of neonates with genetically proven trisomy18, with special attention paid to the efficiency of prenatal diagnostics, associated malformations, and therapeutic dilemmas and outcomes in this group of patients.

Material and methods: We investigated retrospectively the data concerning 20 neonates with trisomy18, admitted to the Department of Neonatal Intensive Care between 2000 and February 2005.

Results: The birth weights ranged from 650g to 2400g, mean 1812g with gestational age (GA) from 27 to 42 weeks, median GA 38 weeks. Signs of intrauterine growth retardation were noticed in 90% of neonates. Trisomy 18 was suspected prenatally in 40 % of cases. Most (80%) of newborns were delivered by way of Caesarean section (92% neonates with prenatally unrecognized chromosomal defects, 62% neonates with suspicion of trisomy18). Seventy percent of cases needed respiratory support immediately after birth. Cardiac defects were present in 90% of cases, central nervous system malformations were diagnosed in 65% of patients, congenital severe defects of digestive system were detected in 25% of patients. Nine surgical operations were performed during hospitalization (4- palliative cardiac surgeries). Six patients survived (30%) the neonatal period and were discharged from the NICU. The median survival of those neonates who died was 20 days. In 3 cases cardiac problems implicated the death of the infants; in others deaths were attributed to multi-organ failure, prematurity and infection.

Conclusion: Prenatal ultrasound screening failed to diagnose most of the fetuses with trisomy 18 in the study group. The incidence of Caesarean section was high among patients with Edwards' syndrome, especially when the chromosomal anomaly was not antenatally suspected. Considering the poor prognosis prompt karyotyping of clinically suspected trisomy 18 is very important because many invasive procedures and surgeries may then be avoided.

(P 50)
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PRENATAL ULTRASOUND IN OBSTETRICAL AND SURGICAL MANAGEMENT OF CONGENITAL DEFECTS/ DEVELOPMENTAL ABNORMALITIES. WHERE ARE WE?
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Aim of the study: Evaluation of the influence of the prenatal ultrasound on obstetric and surgical management in congenital defects/developmental abnormalities.

Material and methods: Obstetrical and surgical files of 67 neonates/infants born in the Department of Feto-Maternal Medicine and then operated in the Department of Surgical Pediatrics and Oncology between 1998 and 2004 due to congenital defects/developmental abnormalities were analyzed. The material was divided into 10 groups with regard to defects of particular systems and then analyzed according to sample sizes, sensitivity of ultrasound imaging, gestational age at diagnosis, age of the pregnant women, previous obstetric history, course of pregnancy, type of delivery and surgical management and outcome.

Results: Prenatal ultrasound was performed in 64 (96%) of fetuses, mean gestational age at diagnosis was 31 weeks, mean age of pregnant women was 26 years, mean gestation time was 37 weeks, mean birth weight of the newborn was 3100g. Defects were recognized in 49 fetuses (74%) and resulted as indication for Cesarean section in 38% of cases. The highest (100%) sensitivity of prenatal ultrasound was found in CNS and urinary tract defects, and 80% in gastrointestinal tract defects. In 19 cases of defects suitable for in utero/ intra partum intervention the prenatal diagnosis was established in 18 cases (sensitivity 95%).

Successful surgical management was performed in 67 newborns/infants according to the standards applied for the particular defects.

Conclusions:
1. Prenatal ultrasound showed high sensitivity in recognition of congenital defects/developmental abnormalities in the fetuses from the own material
2. Earlier than usual recognition of fetal defects should be achieved
3. Cooperation between surgeon and obstetrician is necessary in planning of obstetric and surgical management.
ABNORMALITIES.
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Aim: To evaluate the role of fetal ultrasonography in detection of chromosomal aberrations.
Material and methods: A retrospective study was performed on 23 affected fetuses: with trisomy 21 (8), trisomy 18 (5), trisomy 13 (1), triploidy (2) and Turner syndrome (7). They all were diagnosed prenatally between January 2001 and October 2004 in the Dept. of Perinatal Medicine and Women Diseases, Poznan, Poland. Only in 9 cases we performed the first ultrasound examination before 14 weeks, the remaining 14 fetuses were referred to us in later pregnancy. In all cases anatomical malformations found during ultrasound were indications for invasive methods of kariotyping (AC or PUBS).
Results: 17 of 23 fetuses with abnormal kariotype had more than one malformation detectable on ultrasound. Most common US findings were: heart defects (14/23), shortening of femur (10/23), generalized edema (9/23), IUGR (8/23), cystic hygroma (7/23), ventriculomegaly (6/23), increased nuchal translucency (3/23).
Discussion: A variety of prenatal sonographic findings may be associated with chromosomal abnormalities. Most common anomalies are defects of heart and great vessels. They accompany chromosomal abnormalities in 30-40%.
Other “great” US markers like cystic hygroma, duodenal atresia, omphalocele are less common, but highly correlated with abnormal kariotype. The most useful “small” marker is shortening of FL.
Conclusions: In Poland prenatal biochemical and early ultrasound screening of chromosomal abnormalities is still not obligatory, therefore the awareness of sonographic findings associated with those disorders is very important and should result in an improved detection rate.

(P 52)
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PRENATAL DIAGNOSIS OF CYSTIC HYGROMA. REVIEW OF 9 CASES
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Aim: To compare the prognosis and outcome of fetuses with cystic hygroma and normal or abnormal kariotype.
Material and methods: Nine consecutive fetuses diagnosed with cystic hygroma were evaluated ultrasonographically and kariotyped. All of them were monitored throughout the remainder of the pregnancy. Those who survived were followed-up postnatally.
Results: 6 of 9 fetuses apart from cystic hygroma revealed additional malformations like ascites, hydrothorax, generalized edema, heart defect, oligohydramnion. 5 of 9 were diagnosed before 14 weeks. 7 of 9 fetuses had a kariotype 45X; 2 of 9 were chromosomally normal (46XX and 46XY). All fetuses with Turner kariotype died in utero. Both fetuses with normal kariotype were delivered at term. One required surgical help, in the other the hygroma resolved during neonatal period. The follow-up revealed normal, healthy neonates.
Discussion: Cystic hygroma recognized prenatally can be an ultrasound marker of chromosomal abnormalities. It is an indication for kariotype testing. The most common kariotype is 45X. In those cases, especially if accompanied by additional anatomical malformations, the prognosis is poor. For infants with normal kariotype the prognosis is rather good.
Conclusions: Prenatal ultrasound can help detect severe, often lethal, cases of Turner syndrome.

(P 53)
K Piotrowski, Z Celewicz, S Zajączek
RESULTS OF PRENATAL NON-INVASIVE SCREENING IN PREGNANT WOMEN FROM THE WESTERN POMERANIA REGION OF POLAND
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Between January 2004 and January 2005, 471 pregnant woman in the 1<sup>st</sup> and 2<sup>nd</sup> trimesters of pregnancy were screened with non-invasive USG/biochemical (PAPP-A, f-βHCG, T-HCG, AFP, UE3). Biochemical analyses were individually chosen, depending on CRL and BPD of the fetus. The risk was determined using PRISCA computing program.
Results: A total of 471 cases were analysed, including 121 women above 35 years old. By way of USG only, pathological features were detected in 2 pregnancies. There were one case of trisomy 13 and one ectopia cordis. By way of biochemical tests only, we found 22 cases of higher risk, confirmed then as a trisomy in 10 pregnancies. In the integrated tests we found 21 cases of higher risk, confirmed then as autosomal trisomy in 10 cases and other
Pathologies in 6 cases, in 5 cases normal foetus was diagnosed; two of them were miscarried spontaneously. According to indications from non–invasive tests 18 amniocenteses and 2 cordocentheses were performed. In this sub-group 6 pathologies were confirmed. In nine cases, despite good results of non-invasive screening, invasive prenatal diagnosis was performed (age indications, psychological reasons, etc.). Amniocenteses without non–invasive tests were suggested; one case of trisomy 13 was detected.

Only in one case (congenital nephroblastoma) gross fetal pathology was not detected at the level of non-invasive tests. No complications of procedures were noted.

1. Non-invasive combined screening has a high efficiency in detection of severe foetal pathologies.
2. In spite of advanced age, in all women with normal values of non–invasive screening healthy children were born.
3. Non-invasive prenatal screening is an efficient, low–cost and safe method of detection of pregnancies with a higher risk of major genetic defects and malformations. This is a method of choice in routine population screening.
1) The length of nasal bone and nuchal fold thickness are markers of the highest coefficients in detecting fetal chromosomal aberrations in the second trimester of gestation.

2) The presence of at least two ultrasound markers determines an indication of further diagnosis of fetal chromosomal aberrations.

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PRENATAL DIAGNOSIS OF CROUZON SYNDROME IN THE HIGH-RISK FAMILY

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Crouzon syndrome is an autosomal dominant craniofacial dysostosis. The main features of the syndrome are: craniostenosis, midfacial hypoplasia, proptosis, mandibular prognathism. The syndrome is caused by mutations in the fibroblast growth factor receptor-2 (FGFR2) gene. To date, over 30 mutations in FGFR2 are known. A quarter of them are de novo mutations.

We present a familial case of Crouzon syndrome diagnosed prenatally by ultrasound examination and confirmed by molecular analysis. Three-dimensional ultrasound examination performed in 27-28 Hbd in the 1st and 2nd pregnancy revealed a deformation of temporal region of the skull and dysmorphic features (ocular proptosis, shallow orbits, wide, flat nasal bridge and prognathism). These signs together with data from pedigree analysis have led to suspicion of Crouzon syndrome. The clinical picture assessed after birth varied between the two patients. The analysis of DNA isolated from amniocytes in the 1st and 2nd pregnancy pregnancy revealed the same mutation that found in the father – S267P in 7 exon of the FGFR2 gene. Presented case is one of only a few prenatally diagnosed cases of Crouzon syndrome and it documents the significance of the modern techniques of prenatal visualization – three-dimensional ultrasonography and magnetic resonance in the diagnosis of dysmorphic syndromes. Prenatal molecular diagnostics is the method of choice in high-risk families of Crouzon syndrome.

(MD Pospieszynska)

INDICATIONS FOR PROPHYLAXIS OF CLEFT PALATE ON THE BASIS OF FREQUENCY OF OCCURRENCE OF POTENTIAL CAUSES

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The aim of the work was establishing of indications of prevention of the cleft palate on the ground of frequency of occurrence of most often mentioned potential causes of this defect in literature.

117 children with the cleft palate became the material for this work. All children were applied for orthodontic treatment. In this group was 107 children with cleft lip and palate (Q37), including 40 children with unilateral cleft, 37 with bilateral cleft, 5 children with cleft palate (Q35).

The methodology of the study consisted in compiling information from these children mothers' towards their health and life standard and circumstances of work during pregnancy, also the anamnesis dealt with clefts palate which occurred in their families. The answers were noted down in specially prepared questionnaire.

Results: The age of inquired women reach from 16 to 44 years old. The largest group, consisted of 44 persons, made women between 25 years old and 29 years old. The greater part of group (exactly 102 from 117 inquired mothers) nourished well during pregnancy. Only 15 women (12,8%) submitted defective diet.

In 34 women (36,7%), in 1st trimester of pregnancy occurred persistent vomiting. 37 women (31,7%) suffered in this period of time from different sort of diseases. Most often because in 29 women these were viral or bacterial diseases (in 17 influenza, in 9 common cold and in 3 angina), 8 women suffered from other illnesses, as biliary colic (3), anaemia (3), renal colic (1), and toxaeemia of pregnancy (1). Medicines were taken by 30 women, which is 25,7%. These were most often salicylates and sedatives, more seldom antibiotics, medicines maintaining pregnancy and cholagogic.

Habit of smoking practices 17 women before and during pregnancy, and 23 women only before pregnancy. 37 women (48,7%) worked physically, but only 4 in harmful circumstances.

Remaining women (31) worked intellectually, and only 29 at home.

Familial occurrence of cleft referred to 31 cases, which is 26,5% including in 4 cases (3,4%) this defect occurred in mother, and in 2 cases (1,7%) in father of child with cleft.

Conclusions: On the ground of estimation of frequency of occurrence of factors environmental, which can become the cause of cleft palate it can be accepted, that in prevention this defect it should be laid stress on overcoming these, which occurred most often. These are:
1. Persistent vomiting in 1st trimester of pregnancy, which referred to 36.7% women.
2. Illnesses of mother, which suffered from 31.7% from among them.
3. Medicines taken by women in pregnancy, which took 25.7% from among them.
Moreover familial occurrence of cleft palate in 26.5% examined persons motivates sense of purpose genetic guidance for parents, in whose families are well-known cases of this fault.

(P 58)
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FETAL ABNORMALITIES IN USG AS AN IDICATION TO PRENATAL DIAGNOSIS (PD)
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5085 prenatal cytogenetic tests were performed in the period 1999 – 2004.
In 816 cases (16%) fetal abnormalities detected by USG were the indication to PD. In 157 out of these cases (19%) chromosomal aberrations were found. This constitutes 49% of abnormal karyotypes detected in the overall group. Out of 157 aberrations – 135 were numerical ones: trisomy 18 – 40, trisomy 21 – 37, trisomy 13 – 9, Turner s. – 34, triploidy – 15. Unbalanced structural rearrangements were found in 15 cases.
Among USG abnormal findings most frequent were congenital heart disease (CHD) – 139 cases, hydrocephalus – 102 cases, increased nuchal translucency (NT) was documented in 83 cases.
Out of 68 isolated CHD cases – chromosomal aberrations were found in 15%. In 71 cases with multiple fetal abnormalities, including CHD, chromosome aberrations were found in 50%. No aberrations were found in 55 cases of isolated fetal hydrocephaly. However when hydrocephaly was accompanied by other abnormalities, cytogenetic aberrations constituted 27%.
In 56 cases with increased NT as an only marker of aneuploidy – chromosomal aberrations were found in 13%. However karyotype abnormalities were documented in 19 of 27 cases (71%) of increased NT with other fetal abnormalities.
We observe a steady increase of USG indications to PD: in 1999 – 10%, in 2004 – 24%.

Medical care and case reports:

(P 59)
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THE FOCAL (FOLLOW-UP OF CONGENITAL ANOMALIES LONG-TERM) STUDY
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Ultrasound technology has advanced at a rapid pace and many anomalies that in the past would not have been evident until birth can now be detected during the second trimester of pregnancy. Having identified a structural defect the clinician needs to provide counselling to the expectant parents about the likely effect the anomaly will have on the outcome of their pregnancy and any future health problems the child may face.
Unfortunately our knowledge about the prognosis of many conditions that can be diagnosed using ultrasound technology has not advanced at the same rate as the technology itself. This situation pertains for a whole range of structural congenital anomalies. In many instances there are reasonable estimates of the incidence of the condition and the likely occurrence of stillbirth and complications at birth. However, in many cases there is relatively little, or indeed no, information about the longer term effects of the condition upon the child’s life beyond the neonatal period. Part of this difficulty arises because of the relative rarity of these types of conditions. To accumulate information about sufficient numbers of cases to provide an accurate prognosis is very difficult unless carried out by large referral centres over long periods of time or by population based registers.
Thus, the FOCAL project has been set up to develop a standard methodology for the long-term follow-up of children with structural congenital anomalies or soft-markers; to document and describe their health status in early childhood in terms of quality of life, long term morbidity and mortality and their level of educational achievement; and to make this information widely available for use when counselling expectant parents.

This will be a collaborative project involving the BINOCAR (British Isles Network of Congenital Anomaly) Registers in England and Wales and the National Perinatal Epidemiology Unit (NPEU) in Oxford. The study will be prospective and questionnaire based, assessing the children at the ages of 2 and 7 years. A comparison cohort will also be assessed. The pilot study will commence shortly using diaphragmatic hernia as a model, funded by Newlife (Birth Defects Foundation).

Further details of this study will be presented with a discussion on the problems encountered.

(P 60)
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SOLITARY OR MULTICYSTIC DYSPLASTIC KIDNEY - UROLOGICAL ANOMALIES IN CHILDREN
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The aim of the study was to determine the incidence of associated urological abnormalities in children with unilateral renal agenesis (RA) or multicystic dysplastic kidney (MDK).

Materials and methods: We studied 38 children: 21 with RA and 17 with MDK (10 girls, 28 boys). The congenital anomaly of the urinary tract was suspected in 14 (37%) children on the grounds of the result of prenatally performed USG. In the remaining 24 children the diagnosis of RA/MDK was confirmed postnatally: in 13 (34%) in the first 2-3 days of life, in 11 (29%) at the age of 0.5 to 22 months (average 7.1). The indications for USG study of the abdomen in 24 children were intrauterine infection in 5, premature birth in 2, urinary tract infection in 4, criptorchidism in 1, and abdominal mass in 1. In 11 children RA/MDK were diagnosed in accidentally performed US. The voiding cystourethrography was carried out in 36 (95%) children, the isotopic 99mTc-EC/99mTc-DMSA kidney scan in 29 (67%).

Results: Urological anomalies were present in 11 (29%) children: in 7 (33%) with unilateral RA and in 4 (27%) with MDK. Vesicoureteral reflux was diagnosed in 8 children - in 1 child to ectopic kidney, in 1 to duplicate (Iio in 4, IIIo in 3, IVo in 1); ureterovesical junction obstruction in 2; ureteropelvic junction obstruction in 1.

Conclusions: The diagnosis of renal agenesis or multicystic dysplastic kidney needs further imaging investigation because of coexistence of the congenital anomalies of the urinary tract in over 30% of children.

(P 61)
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Introduction: Congenital cystic adenomatoid malformation of lungs (CCAM) is a rare congenital malformation of the respiratory system. It can be properly treated after birth by the excision of the changed part of the lung (lobe or segment). The final rate of survival depends on the grade of lung hypoplasia, maturity of lungs and/or coexistence of other malformations, prematurity, infections, etc. The aim of the work was to establish the outcome of surgical treatment with CCAM treated in PMMHRI. Material and methods: We assessed 17 neonates with different types of CCAM (type I - 7 neonates, type II – 9 neonates, type III – 1 neonate), who were hospitalized in the Department of Neonatology of PMMHRI in 01.01.1991-31.03.2005. The diagnosis was established based on clinical picture of the malformation, chest X-ray, computed tomography of lungs of the neonate, pathological examination and autopsy. Results: in the analyzed group of neonates successful surgery procedures were carried out in 16 of 17 cases (94.1%). Only in 1 case immediate death after surgery was noted (5.9%). There was a neonate with CCAM type III and the presence of lethal malformation has been established by authopsy. In most cases of neonates with CCAM who underwent the surgery (12/17), total lung lobe resection had been done (70.6%). One neonate required partial lung lobe resection (5.9%) and one required partial and total lung lobe resection (5.9%). Two neonates required additional surgery procedures on the 10th and 30th day of life (11.7%). In 1 of 17 cases lobectomy was bilateral (5.9%). In the group of 7 neonates with CCAM type I surgical procedures were carried out on the average 10.1 day of life. In the group of
neonates with CCAM type II (9 neonates), in 7 cases surgical procedure was done on the average 10.75 day of life, but in 2 cases surgical procedures were carried out later in the 4th and 12th month of life respectively.

Conclusions: 1. In most cases surgical procedures were carried out in the neonatal period (average 10th day of life, 15/17- 88.32%). 2. In all cases, in neonates with CCAM type I and type II, the outcome of surgical procedures was successful. 3. In most cases of the CCAM cystic changes in lungs were one-sided (9/17 left-sided, 7/17 right-sided) but in one case in neonate with CCAP type II cystic changes were situated in both lungs.

(P 62)
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MEDICAL AND GENETIC CONSULTATION OF BABIES WITH DIFFERENT FORMS OF FACE SPLITTING
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Object: estimation of congenital malformations with different forms of face splitting frequency and determination of medical and genetic consultation role concerning this problem.

Volume and Methods. During 1999-2003 72 newborns with harelips and palate fissure and 29 newborns with congenital malformations of eye, ear, face and neck were registered in Kyiv Region in the network of the Special State Genetic Monitoring Program.

Results. The harelips and palate fissure frequency (Q35-Q37) was 1.13 per 1000 born alive in Kyiv Region during 1999-2003 and frequency of congenital malformations of eye, ear, face and neck (Q10-Q18) was 0.46%. These congenital malformations are not lethal, so such fetuses are not eliminated by abortions by medical indications and such frequency is considered to be population frequency.

Compulsory medical and genetic consultation is necessary for babies with different forms of face splitting for estimation of segregative and mutation multipliers of this pathology, calculation of genetic risk for future babies, syndromes description, timely diagnostics of concomitant diseases and improvement of treatment and social adaptation of such children.

(P 63)
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CORRELATION BETWEEN SEX; INTRUTERINE POSITION AND FAMILIAL PREDISPOSITION AND NEOANTAL HIP ULTRASOUND RESULTS
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Aim: To correlate findings of hip ultrasound on day 4-10 of life with sex, intrauterine position and a positive family history for congenital hip anomalies.

Method: The SNIP-study (Survey of Neonates in Pomerania) registered 2256 newborns (2030 term, 226 preterm) between May 2002 and March 2004. Hip ultrasound results of 1043 term and 33 preterm neonates were analyzed. Time of ultrasound was day 4-10 after birth. Preterms were examined when reaching their corrected term gestational age. Ultrasound was done with a 7.5 MHz linear scanner and results were classified according to Graf. Chi-square and Fishers exact test were used for statistical analyzes.

Results: 4.9 % of the screened hips were classified as IIc or higher, 3.1 % were unilateral and 1.7 % bilateral. Incidence was significantly higher in females (6.6 %) than in males (3.2 %). There was no significant difference in intrauterine position or positive family history for hip anomalies with 3.7 % for mothers, 1.2 % of fathers and 2.4 % of siblings positive. There was a higher incidence for congenital hip dysplasia in preterms with 6.1 % which is not significant due to the limited number.

Discussion: Current screening methods miss up to 18 % of the newborns with severe hip dysplasia. We were able to demonstrate that a screening for congenital hip dysplasia with ultrasound is a diagnostic tool even within the first days of life. There is a significant higher incidence of congenital hip dysplasia in females, but in contrast to other studies we found no significant difference in intrauterine position or familial history. Earlier diagnosis and therapy on the base of relevant risk factors might correspond with an improved prognosis and outcome. Further studies are warranted to evaluate the significance in preterms.

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(P 64)
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Objectives: The authors determined the preoperative management and outcome for neonates with congenital diaphragmatic hernia (CDH) in a single inborn population.

Material and methods: The study was made between 1992 and 2002 in the Institute Polish Mothers Memorial Hospital in Lodz. Fifty five term and near term newborn infants (mean gestational age 37.8 weeks; mean birth weight 2843g) were admitted and followed in our unit during all preoperative period. Patients underwent surgery after there was evidence of reduced pulmonary pressure assessed by means ECHO examination. The study population was divided into two groups. The first group (A) consisted of 15 newborns treated with conventional therapy. In the second group (B) there were 40 newborns treated with new techniques (inhaled nitric oxide [NO], high frequency oscillatory ventilation [HFOV]).

Results: CDH was diagnosed prenatally in 26 (47%) patients. A total of 55 associated major anomalies were found in 17 newborns. Surfactant was used in 13, NO in 15, HFOV in 21 patients. In 29 (53%) infants surgical correction was performed. The mean age at surgery was 2.6 days. The total postnatal mortality was 65.5% and 35% after surgery respectively. The comparison of subgroups revealed no statistical differences regarding total mortality before (60% vs. 67%) and after operation (33% vs. 35%).

Conclusions: Although new treatment methods have introduced over last decade, mortality rate with congenital diaphragmatic hernia remains high.

(P 65)

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**CLINICAL AND DIAGNOSTIC ASPECTS OF CONGENITAL BRONCHOGENIC CYST IN A GROUP OF 4. PATIENTS FROM NEONATAL DEPARTMENT OF POLISH MOTHER'S MEMORIAL HOSPITAL RESEARCH INSTITUTE (1991-2005).**

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Introduction: Congenital bronchogenic cyst is a well-known but rare congenital malformation of the respiratory system. The origin of isolated cysts relates to pseudoglandular phase of lung development (7-16 week of gestation). This malformation can be diagnosed in radiological examinations in neonate as a single cyst in lungs situated peripherally or in projection of mediastinum.

The aim of the work: The aim of the work was to establish diagnostic and clinical criteria of the congenital bronchogenic cyst for neonate and child based on postnatal diagnostics in reference center.

Material and methods: It has been analyzed 4 cases of patients with congenital bronchogenic cyst, who were diagnosed and/or treated in Department of Neonatology Polish Mother's Memorial Hospital Research Institute in 01.01.1991 – 31.03.2005. The diagnosis was established based on: clinical picture of the malformation, chest x-ray, computed tomography of lungs of neonate, pathological exam. After the discharge from the Department of Neonatology of PMMHRI neonates remained under the care of many specialist from PMMHRI in the aim of establishing of follow-up results.

Results: In years 1991-2005 diagnosis of congenital bronchogenic cyst was established in 4 cases of patients treated in Department of Neonatology of PMMHRI in Łódź. In 4 cases diagnosis was established based on radiological diagnostics (chest x-ray and computed tomography of lungs) and confirmed by pathological exam (3/4 – 75%). Differential diagnosis included: congenital cystic adenomatoid malformation of lungs (CCAM), enterogenic cysts, bronchopulmonary sequestration, congenital lobar emphysema, diaphragmatic hernia and pneumothorax.

Conclusions: 1. Radiological diagnostics in neonates with congenital bronchogenic cyst is essential because it allows to establish true data regarding this malformation in population. 2. Neonates with diagnosed congenital bronchogenic cyst should be monitored in reference center. 3. Children with the diagnosis of congenital bronchogenic cyst after successful surgery in follow-up have showed normal psycho-physical development and no showed any disturbances in circulatory system.

(P 66)

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SUCCESSFULLY TRANSPLACENTAL THERAPY WITH DIGOXIN IN FETAL ATRIAL FLUTTER

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Atrial flutter is the second most common fetal tachyarrhythmia. Such disturbances can be easily detected by prenatal echocardiography. MATERIAL AND METHODS: We present a case of a 27-week fetus from a woman with a previously unremarkable pregnancy. She was noted to have fetal tachycardia during the routine obstetric exam, with no obvious cause. Fetal echocardiography in the 27th week of gestation resulted in fetal atrial flutter with a 2:1 block, with a rhythm of ventricles 150/min. Hydrops fetalis was not reported. RESULTS: Prenatal echocardiographic examinations in the 28th, 29th, 30th, 32nd, 34th and 37th week of gestation were performed. Transplacental therapy with digoxin was successfully used; occurrence of sinus rhythm was noted. Digoxin level was 1.8 – 2.2ng/mL. RESULTS: In the 37th week of gestation a girl was born with Apgar score of 10, 3250g of weight and 57cm of height. Sinus rhythm was observed. The echocardiographic examination performed on the second day after birth reviled only foramen ovale apertum. CONCLUSIONS: Prenatal echocardiography enables early diagnoses and treats fetal arrhythmias.

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HARLEQUIN ICHTHYOSIS-CASE REPORT AND DIFFICULTIES IN PRENATAL DIAGNOSIS
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The ichthyoses belongs to the group of genodermatosis, characterized by hyperkeratosis and desquamation of epidermidis. Clinical manifestation is changeable and depends on the type of disease. Harlequin foetus is the most severe form of congenital ichthyosis, inherited as an autosomal recessive trait. The dysfunction of epidermis begins prenatally. At present, better care and treatment prolong the length and quality of children’s life. Ultrastructural studies of the skin have revealed characteristic abnormalities in lamellar granule structure and epidermal keratin expression. CASE REPORT: After 37 weeks of gestation, gravida 3, deliver 3, a live male neonate weighing 2900g was delivered. Sonography in the 26th week of gestation showed anomalies of the face. Antenatal karyotyping was made in the 27th week – karyotype 46, XY, 1 qh (+), with a large heterochromatic region of chromosome 1. Cytogenetic examinations of parents revealed mother’s karyotype 46, XX 1 qh (+) and father’s karyotype 46, XY. There had not been any congenital defects in family reports. Prenatal identification was not found. The infant was born in severe condition with features of harlequin ichthyosis. The neonate required intensive neonatological care. On the 4th day after birth the infant was referred to the Department of Neonate Pathology of IP CZD in order to continue care and treatment.

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A CASE OF A FOUR-YEAR-OLD BOY WITH BORJESON-FORSSMAN-LEHMANN SYNDROME
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Borjeson-Forssman-Lehmann syndrome (OMIM 301900) is a very rare disorder inherited as an X-linked recessive genetic trait. Major characteristics of this disorder include an unusual facial appearance, mental retardation, seizures, delayed sexual development, muscle weakness and obesity. The following report concerns a 4-year-old boy with clinical features of severe mental retardation and obesity suggesting BFS syndrome. The patient was the first and only child of healthy unrelated parents who did not reveal genetic problems. In the 26th week of gestation prenatal ultrasound examination revealed microcephaly. The child was born at term following a pregnancy complicated by hypertension and oedema in the 32nd week. His weight at birth was 3950 grams and he was 60 cm long. The head circumference measured 34 cm and Apgar score was 9. Early motor milestones were delayed, in that he sat without support only after 13 months and walked after the age of 4 years. Clinical examination at the age of 4 showed dysmorphic features such as microcephaly, coarse face, narrow forehead, short palpebral fissures, deep set eyes, large and protruding ears, high arched palate. Marked obesity and hypogonadism with small penis and testes were observed. His hands were small with tapering fingers. Karyotyping of peripheral blood leucocytes showed a normal male karyotype (46, XY). MRI of the brain revealed very narrow corpus callosum and small volume of frontal lobes with diminished anterior-posterior diameter. On ophthamological examination atrophy of the optic nerve was revealed. On cardiological examination ventricular septal defect was diagnosed. Concluding the child clinically fit exactly the characteristics of Borjeson-Forssman-Lehmann syndrome.
Laparoscopy was performed in 34 girls aged 12 – 16 with congenital colpatresia. Rokitansky-Küstner-Hauser-syndrome was diagnosed. In all the girls, in addition to morphologically and functionally normal ovaries, lying highly on the lateral wall on the pelvis, uterine horns with the normal, underdeveloped, or rudimentary fallopian tubs were found. In 19 girls rudimentary uterine hours were observed, and in 5 girls large but inactive ones. In 3 girls large uterine horns on one side, and the rudimentary ones on the other side were seen. In 4 girls one – sided ovaries with uterine hours and fallopian tubes were stated. In 3 cases the active uterine horns, being cause of pelvic pain, were surgically removed, and in one girl of them the active horn was a site for the onset of pelvic endometriosis.

(C 70)
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CYSTIC FIBROSIS ASSOCIATED WITH ANAL ATRESIA
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Cystic fibrosis is the most common autosomal recessive genetic defect of one gene CFTR, where a variety of mutations were revealed. Cystic fibrosis is a variable disease and to date the genotype-phenotype correlation has been difficult to clarify. The first symptom of CF is meconium ileus diagnosed in 5-10% of patients with this disease. It is known from literature that cystic fibrosis could be connected with congenital atresia of alimentary tract, especially of the jejunoileal tract. There has been no report of CF with anal atresia present in literature. The authors present a case study of siblings with cystic fibrosis and congenital gastrointestinal defect in one of them. CF was diagnosed in the first infant at 18 months of age because of recurrent respiratory infections and hepatic and hematological problems. The second child of the same parents was born with anal atresia with vaginal fistula. CF was diagnosed at 5 months of age after severe pneumonia. Clinical diagnosis of CF in both siblings was confirmed by the molecular testing of the CFTR gene. Two mutations were revealed in F508 and W1282X. Each of them was diagnosed in siblings in the same pattern: F508 in mother and W1282X in father of children. The prevalence of CF parents, in children with congenital bowel atresia is 6-13%, which is considerably higher than in the normal population. There is still no good explanation for this finding, but it is likely that CF contributes to the development of bowel atresia. The consequence of the defected CFTR gene is the impairment of membrane transport of the chloride ions leading to production of the condense and viscous secretion in all epithelial cells. It is supposed that disturbances in colonic ions secretion in CF reflects the absence of CFTR and suppression of cAMP stimulation in enterocytes.

(P 71)
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EMANUEL SYNDROME
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Emanuel syndrome is caused by a (11;22) (q23;q11.2) translocation. It is the only known recurrent, non-Robertsonian, constitutional translocation in humans, first described in 1980 by Dr. B. Emanuel and E. Zackai. We report a case of a newborn with multiple congenital malformations caused by an unbalanced translocation with an additional derivative chromosome diagnosed in cytogenetic analysis [karyotype: 47, XX+der(22)t(11;22)(q23.3;q11.2)]. The clinical picture of a 6–week–old girl presents typical features of Emanuel syndrome known also as supernumerary der(22)t(11;22) syndrome. The clinical phenotype comprises the following pattern of distinct symptoms: intrauterine hypotrophy, congenital heart defect, cleft palate, dislocation of hip, genital abnormalities in males, hypotonia, severe psychomotor retardation and numerous dysmorphic features i.e. microcephaly, hipertelorism, strabismus, dysplastic and low set ears, preauricular tag or sinus, short nose with prominent tip, broad depressed bridge, micrognathia. Searching for the origin of unbalanced translocation in a newborn we diagnosed a balanced reciprocal translocation in two previous generations. Carriers of the balanced constitutional t(11;22) are phenotypically normal but are at risk of having progeny with supernumerary der(22)t(11;22) syndrome, as a result of malsegregation of the der(22). Authors elucidate the mechanism leading to the unbalanced karyotype seen in the supernumerary der(22) syndrome, which is 3:1 meiosis I malsegregation in the carrier parents. Authors also compare the clinical picture of Emanuel syndrome with other isolated cases of chromosome duplication of 11(q23–qter) and 22(pter-q11).
The main aim was to find the rate and outcome of the congenital heart defect-left heart aplasia. The congenital defect is the most serious and often leads to the death of neonates because of the insufficient blood circulation. The diagnosis can be made during pregnancy or after delivery. At present we expect to have such cases diagnosed in the second trimester of pregnancy. If a pregnant woman belongs to the risk group of congenital heart disease the genetic ultrasound scan should be carried out.

Material and methods. All cases of this heart defect found in the High Risk Pregnancy Unit in 2001-2005 were presented. We found 3 cases of this heart defect. In two cases the congenital malformation was diagnosed after delivery and only in one during pregnancy in the second trimester. All those mothers had no history of heart malformations or risk factors presence. All of them were educated and lived in good conditions. For two of them it was the first pregnancy and delivery. In one case the baby was delivered normally with no heart defect. All babies were delivered between 38 and 39 weeks of pregnancy, one by the spontaneous normal delivery, one by elective caesarean section (because of heart defect) and one by caesarean section because of fetal distress during labour. In two cases the diagnosis was made in two days after delivery. In one case the US examination carried out in the 30th week of pregnancy indicates a serious heart defect, the postnatal diagnosis was as before. All of the newborns were transported to the Pediatric Cardiosurgery Unit of M.U. and operated during the first week after delivery.

Results. All the babies were operated with good results by way of multi-step-operations. In one case the operation was complicated by hydrocephalus and 19 months after birth the baby-boy died unexpectedly. Two of the babies are alive after surgical correction but they require supervision and further operations.

Conclusions. The HLHS is a serious heart congenital malformation often diagnosed after delivery because of lack of sufficient diagnostic system in a the group of healthy women.

Tuberous sclerosis (TS - Bourneville disease) is an autosomal – dominant syndrome, characterized by the development of hamartomas and benign neoplasms involving brain and other tissues. Genetic analysis is rendered complex because there are patients who are obligate carriers of the gene but have no evidence of the disease. Several distinct genetic loci have been identified at which mutations can cause tuberous sclerosis, however, the clinical and pathological features caused by these different genes are indistinguishable.

We present a case of TS in neonatal age, with prenatally diagnosed multiple heart tumors by ultrasound (33 Hbd). A neonate from the 3rd pregnancy with imminent abortion was born by cesarean section with the signs of hypoxia. In prenatal ultrasound examination multiple heart tumors, localized in interventricular septum and free left ventricular wall were diagnosed. The diameter of these tumors did not exceed 2.5 cm, but the diminution of the contractibility of the LV wall was evident. Moreover, the cystic degeneration of the renal cortex was also diagnosed. On the 32nd hour after birth the cardiac arrest took place. The resuscitation was successful, but 6 hours later the next cardiac arrest proved to be fatal. At post mortem the multiple rhabdomyomas of the heart was reported, with additional bilateral polycystic renal cortex degeneration and subependymal giant cell astrocytomas of the brain.

Objective: Patient presentation with sacrococcygeal region tumor described as teratoma with myelomeningocele S1-S2 region.

Case report: Male newborn , gravida III, para III, born via caesarean section in 33 week of gestation with birth weight
1800 g, Apgar score 6 points was admitted to NICU “B” in Polish Mother’s Health Memorial Institute in the first hour of life. Prenatal ultrasound examination performed in 33 week of gestation revealed congenital malformation described as nonhomogenous solid/fluid tumor (75 x 54 x 33 mm) localized in sacrococcygeal region. X-ray examination revealed: rachischisis in sacral region from L5 level with parts of sacral and caudal vertebrae, huge tumor mass in extrasacrococcygeal contour without any other abnormalities in cervical and thoracic parts of spine, vertebral bodies of L4 and L5 blocked, trace of L4/L5 intervertebral disc. In the right side of sacrococcygeal region CT revealed two parts of tumor – upper one with fluid consistency described as 17j. H density and lower part with heterogeneous structure described as 30-35 j. H density. Fluid part was connected with sacral part of spinal canal. In 3rd day of life simultaneous surgical and neurosurgical reconstructive operation was performed. Control ultrasound examination did not revealed postsurgical hydrocephalus. Patient was discharged from our hospital in good condition. Spontaneous movement of lower extremities and function of urethral and anal sphincters are preserved.

Conclusion: In the case of diagnosis of sacrococcygeal region tumor in newborn presence of myelomeningocele should be exclude. There is a possibility of simultaneous surgical and neurosurgical reconstructive operation.

(P 75)
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OCULODENTODIGITAL SYNDROME – A CASE REPORT
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Multiple congenital abnormalities are caused by various genetic and environmental factors. The genetic counselling is essential in each case of a child with anomalies and/or dysmorphic features as well as reporting such children to registers of congenital malformations. In the paper a child with clinical features of oculodentodigital syndrome (ODD) is presented. The autosomal dominant syndrome (OMIM *164200) is characterized by narrow nose with hypoplastic alae and thin nostrils, microcornea with iris anomalies, syndactyly and/or camptodactyly of fingers and enamel hypoplasia. The child was registered to Polish Registry of Congenital Malformations as a child born with syndactyly. During the first visit in genetic department the clinical features of ODD syndrome was observed: short, narrow palpebral fissures, microophthalmia, epicanthus, long thin nose with prominent nasal bridge. This female infant was 3 months old with hipotonia and psychomotoric retardation. No structural abnormalities in internal organs were found. Kariotype was normal. She was the first daughter of young, healthy, unrelated parents. Family history was negative. It is important to consider if so-called isolated syndactyly applicated to any registers is associated with more specific phenotype which allows to diagnose certain syndromes and influence, sometimes even change genetic counselling.

(P 76)
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MACULAR DEGENERATION – A NEW SYMPTOM OF CAUDAL REGRESSION SYNDROME?
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Introduction: The incidence of major congenital malformations among infants of diabetic mothers is two to three times higher than for the nondiabetic population. Congenital anomalies among infants of diabetic mothers include neural tube defects and cardiac, skeletal, gastrointestinal, and pulmonary anomalies. Caudal regression syndrome, although very rare, causes what has been regarded as the most typical associated defects in maternal diabetes. Regarding eye anomalies it is usually stated that there is a characteristic constellation of segmental optic nerve hypoplasia, altitudinal or sector visual field defects and normal visual acuity. Case report: In this paper a child with caudal regression syndrome and macular degeneration is presented. The boy was born from the 5th pregnancy, 3rd delivery in 36th week of gestation. Directly after birth there were diagnosed the following birth defects: bilateral hypoplasia of lower extremities with lack of femoral bones, multiple ribs and vertebral anomalies (spondylolischisis, hemivertebrae), cleft palate, left kidney and right testis agenesis and facial dysmophy. Psychological and intellectual development is normal. Cytogenetic investigations confirmed normal male karyotype. The mother of the child suffers from insulin-dependent diabetes mellitus for over 10 years. At the age of 9 a boy was referred again to the ophthalmologic clinic due to bilateral macular degeneration of the retina, posterior polar cataract, decreased visual acuity and abnormal electroretinographic responses and visual evoked potentials (especially in the right eye). At first, Stargardt disease (juvenile macular degeneration) was suspected, but atypical results of ophthalmoscopy and fluorescein angiography caused that this diagnosis was not confirmed.
Conclusion: Because of atypical clinical picture and no final ophthalmologic diagnosis we suggest that macular degeneration is a new, previously not described, symptom of caudal regression syndrome, and not just the result of coincidence.

(P 77)
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DENTAL TREATMENT STRATEGIES IN CLEIDOCRANIAL DYSPLASIA-A CASE REPORT
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The aim of this study was to describe several aspects of dental treatment in patients with cleidocranial dysplasia. Cleidocranial dysplasia is mainly characterized by a pathognomonic deformity of the skull, a hypoplastic midface, lack of eruption of permanent teeth, supernumerary teeth, defects in the clavicles and multiple other deformities. 40-year-old patient come to dental clinic for treatment of denture pathology with disabled eating, because of anomalous distribution and eruption. Patient gave medical and developmental history with familiar antecedent(mother with similar signs). Patient was examined clinically and radiologically, and his dental status was determined. Dental panoramic radiography is a valuable adjunct in confirming the diagnosis of cleidocranial dysplasia. It was found in this patient supernumerary teeth, dentitio tarda(4 years), impaction of the teeth and follicular cyst. The clinical findings were compared to medical data and case history. Because of advance age of the patient and contraindication for orthodontic treatment only surgical and prosthetic treatment were performed. The therapeutic approach should be based on interdisciplinary cooperation between orthodontists as well as oral and maxillofacial surgeons and prosthetics. Lack of abutment teeth and a difficult maxillary base made prosthetic treatment almost impossible. Earlier intervention will materially reduce the extent of surgical and orthodontic procedures, which have previously been extremely long duration, tedious to the patients and often of limited success. The problems of treating this group of patients are still discussed.

(P 78)
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