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AL GAZALI L

van Haelst MM, Maiburg M, Baujat G, Jadeja S, Monti E, Bland E, Pearce K; Collaborators: **Al-Gazali L**, Aytes P, Bonato A, Chitayat D, Dobbie A, Donnai D, Elmslie F, Ferreira J, Francannet C, Gilbert B, Graham J, Hennekam R, Holder S, Kerr B, Maas S, Megarbane A, Meinecke P, Melancon S, Midro A, Nelson J, Philip N, Reardon W, Reutter H, Santos H, Scambler P, Thauvin C, Todos E, Tolmie J, van Essen T, van Haelst M, Wilkie A, Wilson L. **Fraser Syndrome Collaboration Group, Hennekam RC, Scambler PJ. Molecular study of 33 families with Fraser syndrome new data and mutation review.**

Am J Med Genet A. 2008 Sep 1;146A(17):2252-7.

Molecular Medicine Unit, Institute of Child Health, London, United Kingdom. m.van-haelst@ich.ucl.ac.uk

Fraser syndrome (FS) is an autosomal recessive malformation disorder characterized by cryptophthalmos, syndactyly, and abnormalities of the respiratory and urogenital tract. FS is considered to be the human equivalent of the murine blebbing mutants: in the mouse mutations at five loci cause a phenotype that is comparable to FS in humans, and thus far mutations in two syntenic human genes, FRAS1 and FREM2, have been identified to cause FS. Here we present the molecular analysis of 48 FS patients from 18 consanguineous and 15 nonconsanguineous families. Linkage analysis in consanguineous families indicated

possible linkage to FRAS1 and FREM2 in 60% of the cases. Mutation analysis identified 11 new mutations in FRAS1 and one FREM2 mutation. Manifestations of these patients and previously reported cases with an FRAS1 mutation were compared to cases without detectable FRAS1 mutations to study genotype-phenotype

correlations. Although our data suggest that patients with an FRAS1 mutation have more frequently skull ossification defects and low insertion of the umbilical cord, these differences are not statistically significant. Mutations were identified in only 43% of the cases suggesting that other genes syntenic to murine genes causing blebbing may be responsible for FS as well.

ANNEREN G

Nyström AM, Ekvall S, Berglund E, Björkqvist M, Braathen G, Duchon K, Enell H, Holmberg E, Holmlund U, Olsson-Engman M, Annerén G, Bondeson ML. **Noonan**

and cardio-facio-cutaneous syndromes: two clinically and genetically overlapping disorders. J Med Genet. 2008 Aug;45(8):500-6. Epub 2008 May 2.

Department of Genetics and Pathology, Uppsala University, SE-751 85 Uppsala, Sweden.

BACKGROUND: Noonan syndrome (NS) and cardio-facio-cutaneous syndrome (CFC) are related disorders associated with disrupted RAS/RAF/MEK/ERK signalling. NS, characterised by facial dysmorphism, congenital heart defects and short stature, is caused by mutations in the genes PTPN11, SOS1, KRAS and RAF1. CFC is distinguished from NS by the presence of ectodermal abnormalities and more severe mental retardation in addition to the NS phenotype. The genetic aetiology of CFC was recently assigned to four genes: BRAF, KRAS, MEK1 and MEK2.

METHODS: A comprehensive mutation analysis of BRAF, KRAS, MEK1, MEK2 and SOS1 in 31 unrelated patients without mutations in PTPN11 is presented.

RESULTS: Mutations were identified in seven patients with CFC (two in BRAF, one in KRAS, one in MEK1, two in MEK2 and one in SOS1). Two mutations were novel: MEK1 E203Q and MEK2 F57L. The SOS1 E433K mutation, identified in a patient diagnosed with CFC, has previously been reported in patients with NS. In one patient with NS, we also identified a mutation, BRAF K499E, that has previously been reported in patients with CFC. We thus suggest involvement of BRAF in the pathogenesis of NS also.

CONCLUSIONS: Taken together, our results indicate that the molecular and clinical overlap between CFC and NS is more complex than previously suggested and that the syndromes might even represent allelic disorders. Furthermore, we suggest that the diagnosis should be refined to, for example, NS-PTPN11-associated or CFC-BRAF-associated syndromes after the genetic defect has been established, as this may affect the prognosis and treatment of the patients.

Wentzel C, Fernström M, Ohrner Y, Annerén G, Thuresson AC. **Clinical variability of the 22q11.2 duplication syndrome.** Eur J Med Genet. 2008 Jul 29. [Epub ahead of print]

Department of Genetics and Pathology, Uppsala University, Dag Hammarskjolds väg 20, SE-751 85 Uppsala, Sweden.

The 22q11.2 duplication syndrome is an extremely variable disorder with a phenotype ranging from normal to learning disability and congenital defects. Both patients with a de novo 22q11.2 duplication and patients in whom the duplication has been inherited from a phenotypically normal parent have been reported. In this study we present two familial cases with a 3Mb 22q11.2 duplication detected by array-CGH. We also review the findings in 36 reported cases with the aim of delineating the phenotype of the 22q11.2 duplication syndrome. In a majority of the reported cases where parents have been tested, the duplication seems to

have been inherited from a normal parent with minor abnormalities. With this in mind we recommend that family members of patients with a 22q11.2 duplication to be tested for this genetic defect.

BAKKER M

Bakker MK, Kölling P, van den Berg PB, de Walle HE, de Jong van den Berg LT. **Increase in use of selective serotonin reuptake inhibitors in pregnancy during the last decade, a population-based cohort study from the Netherlands.** Br J Clin Pharmacol. 2008 Apr;65(4):600-6. Epub 2007 Oct 22.

EUROCAT registration of congenital anomalies, Department of Genetics, University Medical Centre Groningen, University of Groningen, Groningen, the Netherlands.

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT:

Recently, the use of selective serotonin reuptake inhibitors (SSRIs), particularly paroxetine, in pregnancy has been associated with an increased risk on specific birth defects or other adverse pregnancy outcomes. However, the extent of SSRI use in pregnancy is largely unknown.

WHAT THIS STUDY ADDS:

In the last decade the use of SSRIs in the year preceding delivery has increased twofold. This increase runs parallel with the increase in use of SSRIs among women of fertile age. Paroxetine is one of the most commonly used SSRIs. Only recently have sufficient data become available on the use of paroxetine to detect moderate increased risks for specific malformations. The safety of SSRIs which are less frequently used is not yet established. Case-control birth defect-monitoring systems may be helpful in providing safety and risk estimates that become more precise as data accumulate for these drugs. AIMS: Recent case-control studies suggest a relationship between the use of selective serotonin reuptake inhibitors (SSRIs) and the occurrence of birth defects and other adverse pregnancy outcomes. The aim was to determine the extent of the use of SSRIs before and during pregnancy and its trend over the years 1995-2004 in the Netherlands.

METHODS: The study was performed with data from a population-based prescription database. Within this database, women giving birth to a child between 1995 and 2004 were identified. The exposure rate and 95% confidence interval (CI) were calculated as the number of pregnancies per 1000 that were exposed to an SSRI in a defined period (per trimester or in the year preceding delivery). Exposure rates were calculated for 2-year periods: 1995/1996, 1997/1998, 1999/2000, 2001/2002 and 2003/2004. Trends in exposure rates were analysed using the chi(2) test for trend. RESULTS: Included were 14,902 pregnancies for which complete pharmacy records were available from 3 months before pregnancy until delivery. A total of 310 pregnancies were exposed to an SSRI in the year preceding

delivery. The exposure rate increased from 12.2 (95% CI 7.0, 19.8) in 1995/1996 to 28.5 (95% CI 23.0, 34.9) in 2003/2004.

CONCLUSION: There has been a significant increase in the use of SSRIs among pregnant women in the Netherlands over the last 10 years, parallel with the increase in exposure in women of fertile age. In light of the recent warnings about the use of SSRIs in pregnancy, healthcare professionals should be careful in prescribing SSRIs to women planning a pregnancy.

BOWER C

Bourke J, Ricciardo B, Bebbington A, Aiberti K, Jacoby P, Dyke P, Msall M, Bower C, Leonard H. **Physical and mental health in mothers of children with Down syndrome.** J Pediatr. 2008 Sep;153(3):320-6. Epub 2008 Apr 23.

Telethon Institute for Child Health Research, Centre for Child Health Research, University of Western Australia, Perth, Western Australia.

OBJECTIVE: To identify the relationship between characteristics of the child with Down syndrome and the health of their mother.

STUDY DESIGN: Families with a child/young adult with Down syndrome (<25 years) provided information related to the health of the child, functioning and behavior, and the health and well-being of the mother (n = 250).

RESULTS: The mean physical health score of mothers was 50.2 (SD = 9.6). Factors associated with lower mean physical health scores were as follows: child having a current heart problem (P = .036), a higher body mass index (P = .006), and higher (poorer) scores on the Developmental Behavior Checklist. Better physical health scores were seen in mothers whose children required no help/supervision in learning new skills (P = .008) and domestic tasks (P = .014). The mean mental health score of mothers was 45.2 (SD = 10.6), significantly lower than the norm of 50 (P < .0001). Associated child factors included current ear problems (P = .079), muscle/bone problems (P = .004), >4 episodes of illness in past year (P = .016), and higher scores on the DBC (P < .0001).

CONCLUSIONS: The most important predictors of maternal health were children's behavioral difficulties, everyday functioning and current health status. Mothers of children with Down syndrome appear to experience poorer mental health and may require greater support and services to improve behavior management skills for their child and their own psychological well-being.

CANFIELD MA

Boulet SL, Yang Q, Mai C, Kirby RS, Collins JS, Robbins JM, Meyer R, Canfield MA, Mulinare J; National Birth Defects Prevention Network. **Trends in the postfortification prevalence of spina bifida and anencephaly in the United States.** Birth Defects Res A Clin Mol Teratol. 2008 Jul;82(7):527-32.

National Center on Birth Defects and Developmental Disabilities, CDC, Atlanta, Georgia 30333, USA. sboulet@cdc.gov

BACKGROUND: The prevalence of NTDs in the US declined significantly after mandatory folic acid fortification; however, it is not known if the prevalence of NTDs has continued to decrease in recent years relative to the period immediately following the fortification mandate.

METHODS: Population-based data from 21 birth defects surveillance systems were used to examine trends in the birth prevalence of spina bifida and anencephaly during 1999-2000, 2001-2002, and 2003-2004.

Prevalence data were stratified by non-Hispanic White, non-Hispanic Black, and Hispanic race or ethnicity. Prevalence ratios were calculated by dividing the birth prevalences during the later time periods (2001-2002 and 2003-2004) by the birth prevalences during 1999-2000.

RESULTS: During 1999-2004, 3,311 cases of spina bifida and 2,116 cases of anencephaly were reported. Hispanic infants had the highest prevalences of NTDs for all years. For all infants, the combined birth prevalences of spina bifida and anencephaly decreased 10% from the 1999-2000 period to the 2003-2004 period. The decline in spina bifida (3%) was not significant; however the decline in anencephaly (20%) was statistically significant.

CONCLUSIONS: While the prevalences of spina bifida and anencephaly in the United States have declined since folic acid fortification in the food supply began, these data suggest that reductions in the prevalence of anencephaly continued during 2001-2004 and that racial and ethnic and other disparities remain.

CASTILLA EE

Orioli IM, Mastroiacovo P, López-Camelo JS, Saldarriaga W, Isaza C, Aiello H, Zarante I, Castilla EE. **Clusters of sirenomelia in South America.** Birth Defects Res A Clin Mol Teratol. 2008 Aug 19. [Epub ahead of print]

ECLAMC: Latin-American Collaborative Study of Congenital Malformations, at Departamento de Genética, Universidade Federal do Rio de Janeiro, Brazil.

BACKGROUND: One hospital in the city of Cali, Colombia, of the ECLAMC (Latin-American Collaborative Study of Congenital Malformations) network, reported the unusual occurrence of four cases of sirenomelia within a 55-day period.

METHODS: An ECLAMC routine for cluster evaluation (RUMOR) was followed that included: calculations of observed/expected ratios, site visits, comparison with comprehensively collected local, South American, and worldwide data, cluster analysis, and search for risk factors.

RESULTS: All four Cali sirenomelia cases were born to mothers living in a 2 km(2) area, in neighboring communes, within the municipality of Cali. Considering the total births of the city of Cali as the denominator, and based on ECLAMC baseline birth prevalence rates (per 100,000) for sirenomelia (2.25, 95% CI: 2.66, 3.80), the

cluster for this congenital abnormality was unlikely to have occurred by chance (observed/expected ratio =5.77; 95% CI: 1.57-14.78; p = .002). No consistent common factor was identified,

but vicinity to an open landfill as the cause could not be rejected. Another ECLAMC hospital in San Justo, Buenos Aires, Argentina, reported three further cases but these did not seem to constitute a nonrandom cluster.

CONCLUSIONS: The methodology used to evaluate the two possible clusters of sirenómelia determined

that the Cali sirenómelia cluster was unlikely to have occurred by chance whereas the sirenómelia cluster from San Justo seemed to be random. Birth Defects Research (Part A) 2008.

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Castilla EE, Mastroiacovo P, Orioli IM. **Gastroschisis: international epidemiology and public health perspectives.** Am J Med Genet C Semin Med Genet. 2008 Aug 15;148C(3):162-79.

ECLAMC/GENETICA/FIOCRUZ, Av. Brasil 4365, Pav. 26, sala 617, 21045-900 Rio de Janeiro, Brazil. castilla@centroin.com.br

Gastroschisis offers the intriguing epidemiological situation of a pandemic, strongly associated with very low maternal age. Identifying gastroschisis, and distinguishing it from the other abdominal wall defects, is theoretically easy but difficult in practice. The baseline birth prevalence of gastroschisis before the pandemic was approximately 1 in 50,000 births and has increased since between 10- and 20-fold. In many populations worldwide, it is still increasing. Such increasing prevalence and the association with very low maternal age are well proven, but the interaction between these two findings remains unknown.

Geographic gradients (decreasing prevalence from North to South) are clear in Continental Europe and suggestive in Britain and Ireland. Gastroschisis seems more frequent in Caucasians compared to African Blacks and Orientals, and in Northern compared to Southern Europeans. These observations indicate the need for investigating gene-environment interactions. Since the global human situation is marked by inequalities among as well as within countries, the medical care and public health impact of gastroschisis varies widely among regions and social strata. The postnatal benefits of prenatal diagnosis of gastroschisis include family awareness; adequate planning of delivery with alerted obstetrical, pediatric, and surgical staff; optimal risk categorization, and personalized protocol for action. The increasing prevalence of gastroschisis combined with improved medical techniques to reduce morbidity and mortality are also increasing the burden and costs of this anomaly on health systems.

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Weinberg SM, Brandon CA, McHenry TH, Neiswanger K, Deleyiannis FW, de Salamanca JE, Castilla EE, Czeizel AE, Vieira AR, Marazita ML. **Rethinking isolated**

cleft palate: evidence of occult lip defects in a subset of cases. Am J Med Genet A. 2008 Jul 1;146A(13):1670-5.

Center for Craniofacial and Dental Genetics, School of Dental Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania 15090, USA.

Emerging research suggests that subepithelial defects of the upper lip musculature are part of the phenotypic spectrum of cleft lip and/or palate (CL/P) and may represent an occult, subclinical manifestation of the anomaly. The present study investigates whether similar occult lip defects are present in individuals affected with isolated cleft palate (CP). To this end, upper lip ultrasounds of 33 CP cases (12 males, 21 females) were evaluated retrospectively for the presence of discontinuities (i.e., breaks) within the orbicularis oris muscle (OOM). In four CP cases (2 males, 2 females), distinct discontinuities of the OOM were identified. Of the remaining CP individuals, 23 demonstrated normal lip morphology on ultrasound (7 males, 16 females), while, in 6 cases (3 males, 3 females), a definitive evaluation was not possible. As CP and CL/P are traditionally thought to be etiologically distinct, these findings raise the possibility that some CP cases may be misclassified. Such diagnostic errors could have important implications for recurrence risk estimation and studies aimed at discovering etiology.

CORREA A

Waller DK, Correa A, Vo TM, Wang Y, Hobbs C, Langlois PH, Pearson K, Romitti PA, Shaw GM, Hecht JT.

The population-based prevalence of achondroplasia and thanatophoric dysplasia in selected regions of the US. Am J Med Genet A. 2008 Sep 15;146A(18):2385-9.

Houston Health Science Center, The University of Texas, Houston, Texas 77030, USA.
kim.waller@uth.tmc.edu

There have been no large population-based studies of the prevalence of achondroplasia and thanatophoric dysplasia in the United States. This study compared data from seven population-based birth defects monitoring programs in the United States. We also present data on the association between older paternal

age and these birth defects, which has been described in earlier studies. The prevalence of achondroplasia ranged from 0.36 to 0.60 per 10,000 livebirths (1/27,780-1/16,670 livebirths). The prevalence of thanatophoric dysplasia ranged from 0.21 to 0.30 per 10,000 livebirths (1/33,330-1/47,620 livebirths). In Texas, fathers that were 25-29, 30-34, 35-39, and ≥ 40 years of age had significantly increased rates of de novo achondroplasia among their offspring compared with younger fathers. The adjusted prevalence odds ratios were 2.8 (95% CI; 1.2, 6.7), 2.8 (95% CI; 1.0, 7.6), 4.9 (95% CI; 1.7, 14.3), and 5.0 (95% CI;

1.5, 16.1), respectively. Using the same age categories, the crude prevalence odds ratios for de novo cases of thanatophoric dysplasia in Texas were 5.8 (95% CI; 1.7, 9.8), 3.9 (95% CI; 1.1, 6.7), 6.1 (95% CI; 1.6, 10.6), and 10.2 (95% CI; 2.6, 17.8),

respectively. These data suggest that thanatophoric dysplasia is one-third to one-half as frequent as achondroplasia. The differences in the prevalence of these conditions across monitoring programs were consistent with random fluctuation. Birth defects monitoring programs may be a good source of ascertainment for population-based studies of achondroplasia and thanatophoric dysplasia, provided that diagnoses are confirmed by review of medical records.

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Correa A, Gilboa SM, Besser LM, Botto LD, Moore CA, Hobbs CA, Cleves MA, Riehle-Colarusso TJ, Waller DK, Reece EA. **Diabetes mellitus and birth defects.** Am J Obstet Gynecol. 2008 Jul 30. [Epub ahead of print]

Division of Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA.

OBJECTIVE:

The purpose of this study was to examine associations between diabetes mellitus and 39 birth defects. **STUDY DESIGN:**

This was a multicenter case-control study of mothers of infants who were born with (n = 13,030) and without (n = 4895) birth defects in the National Birth Defects Prevention Study (1997-2003).

RESULTS: Pregestational diabetes mellitus (PGDM) was associated significantly with noncardiac defects (isolated, 7/23 defects; multiples, 13/23 defects) and cardiac defects (isolated, 11/16 defects; multiples, 8/16 defects). Adjusted odds ratios for PGDM and all isolated and multiple defects were 3.17 (95% CI, 2.20-4.99) and 8.62 (95% CI, 5.27-14.10), respectively. Gestational diabetes mellitus (GDM) was associated with fewer noncardiac defects (isolated, 3/23 defects; multiples, 3/23 defects) and cardiac defects (isolated, 3/16 defects; multiples, 2/16 defects). Odds ratios between GDM and all isolated and multiple defects were 1.42 (95% CI, 1.17-1.73) and 1.50 (95% CI, 1.13-2.00), respectively. These associations were limited generally to offspring of women with prepregnancy body mass index ≥ 25 kg/m².

CONCLUSION:

PGDM was associated with a wide range of birth defects; GDM was associated with a limited group of birth defects.

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Reller MD, Strickland MJ, Riehle-Colarusso T, Mahle WT, Correa A. **Prevalence of Congenital Heart Defects in Metropolitan Atlanta, 1998-2005.** J Pediatr. 2008 Jul 25. [Epub ahead of print]

Oregon Health and Science University (M.R.), Portland, OR.

OBJECTIVE: To determine an accurate estimate of the prevalence of congenital heart defects (CHD) using current standard diagnostic modalities.

STUDY DESIGN:

We obtained data on infants with CHD delivered during 1998 to 2005 identified by the Metropolitan Atlanta Congenital Defects Program, an active, population-based, birth defects surveillance system. Physiologic shunts in infancy and shunts associated with prematurity were excluded. Selected infant and maternal characteristics of the cases were compared with those of the overall birth cohort.

RESULTS:

From 1998 to 2005 there were 3 981 400 births, of which 3240 infants had CHD, for an overall prevalence of 81.4/10 000 births. The most common CHD were muscular ventricular septal defect, perimembranous ventricular septal defect, and secundum atrial septal defect, with prevalence of 27.5, 10.6, and 10.3/10 000 births, respectively. The prevalence of tetralogy of Fallot, the most common cyanotic CHD, was twice that of transposition of the great arteries (4.7 vs 2.3/10 000 births). Many common CHD were associated with older maternal age and multiple-gestation pregnancy; several were found to vary by sex.

CONCLUSIONS:

This study, using a standardized cardiac nomenclature and classification, provides current prevalence estimates of the various CHD subtypes. These estimates can be used to assess variations in prevalence across populations, time, or space.

DE VIGAN C

Khoshnood B, De Vigan C, Blondel B, Vodovar V, Cadio E, Goffinet F. **Long-term trends for socio-economic differences in prenatal diagnosis of Down syndrome: diffusion of services or persistence of disparities?** BJOG. 2008 Aug;115(9):1087-95. Epub 2008 May 30.

INSERM, UMR S149, IFR 69, Epidemiological Research Unit on Perinatal and Women's Health, Villejuif, France. babak.khoshnood@inserm.fr

OBJECTIVE:

To assess long-term trends in disparities for prenatal diagnosis of Down syndrome in relation to policy changes.

DESIGN:

Population-based observational study.

SETTING: Paris.

POPULATION: Residents of Paris who gave birth or had a termination of pregnancy in Paris during 1983-2003 (approximately 23,000 births per year).

METHODS:

Using population-based data from the Paris Registry of Congenital Malformations on 1934 cases of Down syndrome, we assessed differences in prenatal diagnosis proportions by maternal profession and geographical origin for the years 1983-2003. Analyses included locally weighted scatter plot smoother curves and binomial regression.

MAIN OUTCOME MEASURE:

Trends in proportion of Down syndrome cases diagnosed prior to birth for different maternal occupation groups and women of different geographical origins.

RESULTS:

The proportion of prenatally diagnosed cases increased substantially, reaching to about 85-90% of cases in 2003 for most socio-economic groups. This increase was accompanied by a significant decrease in disparities in prenatal diagnosis. Nonetheless, the proportion of prenatally diagnosed cases remained 12% lower for women without a profession compared with those in the highest occupational category (maternal age-adjusted risk difference -12.0%, 95% CI -17.1 to -6.9).

CONCLUSIONS:

Together with the implementation of policies aimed at providing access to prenatal screening for all women, socio-economic differences in prenatal diagnosis of Down syndrome decreased over time. These trends need to be monitored, particularly in light of technical advances and alternative strategies for prenatal testing. However, while monitoring the proportion of cases with prenatal diagnosis is important, the ideal evaluation of prenatal testing programmes should also include measures of informed choice.

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Verret C, Jutand MA, De Vigan C, Bégassat M, Bensefa-Colas L, Brochard P, Salamon R. **Reproductive health and pregnancy outcomes among French gulf war veterans**. BMC Public Health. 2008 Apr 28;8:141.

Laboratory of Occupational and Environmental Health, Victor Segalen Bordeaux 2 University, Bordeaux, France. catherine.verret@wanadoo.fr

BACKGROUND:

Since 1993, many studies on the health of Persian Gulf War veterans (PGWVs) have been undertaken. Some authors have concluded that an association exists between Gulf War service and reported infertility or miscarriage, but that effects on PGWV's children were limited. The present study's objective was to describe the reproductive outcome and health of offspring of French Gulf War veterans.

METHODS: The French Study on the Persian Gulf War (PGW) and its Health Consequences is an exhaustive cross-sectional study on all French PGWVs conducted from 2002 to 2004. Data were collected by postal self-administered questionnaire. A case-control study nested in this cohort was conducted to evaluate the link between PGW-related exposures and fathering a child with a birth defect.

RESULTS:

In the present study, 9% of the 5,666 Gulf veterans who participated reported fertility disorders, and 12% of male veterans reported at least one miscarriage among their partners after the PGW. Overall, 4.2% of fathers reported at least one child with a birth defect conceived after the mission. No PGW-related exposure was associated with any birth defect in children fathered after the PGW mission. Concerning the reported health of children born after the PGW, 1.0% of children

presented a pre-term delivery and 2.7% a birth defect. The main birth defects reported were musculoskeletal malformations (0.5%) and urinary system malformations (0.3%). Birth defect incidence in PGWV children conceived after the mission was similar to birth defect incidence described by the Paris Registry of Congenital Malformations, except for Down syndrome (PGWV children incidence was lower than Registry incidence).

CONCLUSION:

This study did not highlight a high frequency of fertility disorders or miscarriage among French PGW veterans. We found no evidence for a link between paternal exposure during the Gulf War and increased risk of birth defects among French PGWV children.

DORAY B

Arch Pediatr. 2008 Jun;15(5):507-9.

[Feasibility of the foetal alcohol syndrome surveillance]

[Article in French]

Bloch J, Cans C, de Vigan C, de Brosses L, Doray B, Larroque B, Perthus I.

Département des maladies chroniques et des traumatismes, Institut de veille sanitaire, 12, rue du Val-d'Osne, 94415 Saint-Maurice cedex. j.bloch@invs.sante.fr

FELDKAMP M

Feldkamp ML, Botto LD. **Developing a research and public health agenda for gastroschisis: how do we bridge the gap between what is known and what is not?** Am J Med Genet C Semin Med Genet. 2008 Aug 15;148C(3):155-61.

Division of Medical Genetics, University of Utah Health Sciences Center, 2C 402 SOM, 50 North Medical Drive, Salt Lake City, UT 84132, USA.
marcia.feldkamp@hsc.utah.edu

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Sadler TW, Feldkamp ML. **The embryology of body wall closure: relevance to gastroschisis and other ventral body wall defects.** Am J Med Genet C Semin Med Genet. 2008 Aug 15;148C(3):180-5.

tsadler@3riversdbs.net

During the 3rd and 4th weeks post-fertilization (5 and 6 weeks from the last normal menstrual period [LNMP]), the human embryo is transformed from a flat disc-shaped organism into the classic shape of an embryo in the "fetal" position. This change is effected by simultaneously rolling the top layer of the disc, the ectoderm, into the neural tube and the bottom layers of the disc, the endoderm and mesoderm, into the gut tube and body wall, respectively. In this manner, the flat disc is transformed into two tubes, one dorsal to the other, surrounded by supporting structures in the body wall. If closure of the neural tube fails, then neural tube defects (NTDs), such as anencephaly and spina bifida, occur; if closure of the ventral body wall fails, then ventral body wall defects, such as ectopia cordis, gastroschisis, and bladder and cloacal exstrophy, occur. Interestingly, no known closure defects have been described for the gut tube. Note, however, that all of the closure defects that do occur have their origins early in gestation during the third and fourth weeks of development.

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Bitsko RH, Reefhuis J, Louik C, Werler M, Feldkamp ML, Waller DK, Frias J, Honein MA; National Birth Defects Prevention Study. **Periconceptual use of weight loss products including ephedra and the association with birth defects.** Birth Defects Res A Clin Mol Teratol. 2008 Aug;82(8):553-62.

Division of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, Atlanta, Georgia 30333, USA.
dvk2@cdc.gov

BACKGROUND:

Weight loss products are frequently used by reproductive-aged women and these products may be taken (inadvertently or intentionally) during pregnancy. This study assessed the association between periconceptual use of weight loss products and major structural birth defects.

METHODS:

Mothers of infants with birth defects (case infants) and a random sample of livebirths (control infants) born during the period 1998-2003 in 10 states participated in the National Birth Defects Prevention Study. Adjusted ORs (aORs) for the association between self-reported use of weight loss products and 23 categories of birth defects were calculated.

RESULTS:

Mothers of control infants (2.4%) and 2.6% of mothers of case infants reported periconceptual use of weight loss products; 1.2% of mothers of control infants and 1.3% of mothers of case infants reported using an ephedra-containing product. Use of any weight loss product was associated with anencephaly (aOR 2.6; 95% CI: 1.3-5.3), dextro-transposition of the great arteries (aOR 2.1; 95% CI: 1.1-4.3), and aortic stenosis (aOR 3.4; 95% CI: 1.5-7.9).

Use of products containing ephedra showed an increased aOR with anencephaly (aOR 2.8; 95% CI: 1.0-7.3), while other weight loss products were associated with

dextro-transposition of the great arteries (aOR 1.8; 95% CI: 1.2-2.7), and aortic stenosis (aOR 2.1; 95% CI: 1.3-3.5).

CONCLUSIONS:

These results suggest an association between periconceptional use of weight loss products and certain birth defects but the possible mechanism is not clear. This is the first finding of such an association and, because we examined a large number of exposure-outcome associations in a hypothesis-generating analysis, these results might have been due to chance.

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Feldkamp ML, Reefhuis J, Kucik J, Krikov S, Wilson A, Moore CA, Carey JC, Botto LD. **Case-control study of self reported genitourinary infections and risk of gastroschisis: findings from the national birth defects prevention study, 1997-2003.** BMJ. 2008 Jun 21;336(7658):1420-3. Epub 2008 Jun 16.

Comment in:

BMJ. 2008 Jun 21;336(7658):1386-7.

Division of Medical Genetics, Department of Pediatrics, University of Utah Health Sciences Center, Salt Lake City, UT 84132, USA. marcia.feldkamp@hsc.utah.edu

OBJECTIVE:

To assess the association between genitourinary infections in the month before conception to the end of the first trimester and gastroschisis.

DESIGN:

Case-control study with self reported infections from a computer assisted telephone interview. SETTING: National birth defects prevention study, a multisite, population based study including 10 surveillance systems for birth defects in the United States.

PARTICIPANTS: Mothers of 505 offspring with gastroschisis and 4924 healthy liveborn infants as controls. MAIN OUTCOME MEASURE:

Adjusted odds ratios for gastroschisis with 95% confidence intervals.

RESULTS:

About 16% (n=81) of case mothers and 9% (n=425) of control mothers reported a genitourinary infection in the relevant time period; 4% (n=21) and 2% (n=98) reported a sexually transmitted infection and 13% (n=67) and 7% (n=338) reported a urinary tract infection, respectively. Case mothers aged <25 years reported higher rates of urinary tract infection alone and in combination with a sexually transmitted infection compared with control mothers. In women who reported both types of infection, there was a greater risk of gastroschisis in offspring (adjusted odds ratio 4.0, 95% confidence interval 1.4 to 11.6).

CONCLUSION:

There is a significant association between self reported urinary tract infection plus sexually transmitted infection just before conception and in early pregnancy and gastroschisis.

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Byrne JL, Feldkamp ML. **Seven-week embryo with gastroschisis, multiple anomalies, and physiologic hernia suggests early onset of gastroschisis.** Birth Defects Res A Clin Mol Teratol. 2008 Apr;82(4):236-8.

Department of Obstetrics and Gynecology, Division of Maternal Fetal Medicine, University of Utah Health Sciences Center, Salt Lake City, Utah 84132, USA.
jan.byrne@hsc.utah.edu

Gastroschisis is an increasingly common birth defect involving the development of the ventral body wall. Extrusion of the bowel is usually paraumbilical, usually right sided, and associated anomalies are less common than in omphalocele. Recently, hypotheses regarding the timing of the typical gastroschisis defect have come into question. Unlike previous theories, Feldkamp et al. (2007) has postulated that gastroschisis occurs much earlier in development, before abdominal wall closure, which is completed by about 35 days postconception. We present a case of a spontaneously aborted dysmorphic embryo which exhibits features of the normal physiologic herniation of the midgut as well as gastrochisis. The co-existence of the abdominal wall defect in this abnormal embryo with the physiologic hernia supports the early development of this defect and also illustrates the causal heterogeneity of gastroschisis.

HALLIDAY J

Herlihy AS, Halliday J. **Is paternal age playing a role in the changing prevalence of Klinefelter syndrome?** Eur J Hum Genet. 2008 May 21. [Epub ahead of print]

[1] 1Public Health Genetics, Murdoch Childrens Research Institute, Parkville, Victoria, Australia [2] 2Andrology Australia, Clayton, Victoria, Australia.

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Fernando S, Breheny S, Jaques AM, Halliday JL, Baker G, Healy D. **Preterm birth, ovarian endometriomata, and assisted reproduction technologies.** Fertil Steril. 2008 Mar 31. [Epub ahead of print]

Department of Obstetrics and Gynecology, Monash University, Clayton, Victoria, Australia.

OBJECTIVE:

To report preterm birth and small for gestational age (SGA) rates from assisted reproduction technologies (ART) patients with ovarian endometriomata compared with control groups.

DESIGN: Retrospective cohort study.

SETTING:

Tertiary university affiliated ART center and Perinatal Data Collection Unit (PDCU).

PATIENT(S):

Every woman who had an ART singleton baby born between 1991 and 2004 had her database record assessed (N = 4382). Control groups included 1201 singleton babies from ART patients without endometriosis and 2400 randomly selected women from the PDCU database of 850,000 births. INTERVENTION(S):

There were 95 singleton ART babies from patients with ovarian endometriomata and 535 ART singleton babies from patients who had endometriosis but no ovarian endometriomata.

MAIN OUTCOME MEASURE(S): Preterm birth rates and SGA birth rates.

RESULT(S): Preterm birth rate increased only in the ovarian endometriomata group when compared with community birth records (n = 850,000). Furthermore, ART patients with ovarian endometriomata had a statistically significantly increased likelihood of having a SGA baby when compared with other forms of endometriosis.

CONCLUSION(S): Rates of preterm birth and SGA babies doubled in infertility patients with ovarian endometriomata who required ART.

LOWRY RB

De Wals P, Tairou F, Van Allen MI, Lowry RB, Evans JA, Van den Hof MC, Crowley M, Uh SH, Zimmer P, Sibbald B, Fernandez B, Lee NS, Niyonsenga T. **Spina bifida before and after folic acid fortification in Canada.** Birth Defects Res A Clin Mol Teratol. 2008 Jul 24. [Epub ahead of print]

Department of Social and Preventive Medicine, Laval University, Quebec City, QC, Canada.

BACKGROUND:

In 1998, fortification of a large variety of cereal products with folic acid became mandatory in Canada. A multicentric study was carried out to assess the impact of this policy on the frequency of NTDs. The present analysis focused on spina bifida.

METHODS:

The study population included approximately 2 million livebirths, stillbirths, and terminations of pregnancies because of fetal anomalies among women residing in seven Canadian provinces, from 1993 to 2002. Spina bifida cases were divided according to the upper limit of the defect: upper (cranial, cervical, or thoracic) and lower (lumbar or sacral) defects. Based on published results of red blood cell folate tests, the study period was divided into prefortification, partial fortification, and full fortification periods.

RESULTS:

A total of 1,286 spina bifida cases were identified: 51% livebirths, 3% stillbirths, and 46% terminations. Prevalence decreased from 0.86/1,000 in the prefortification to 0.40 in the full fortification period, while the proportion of upper defects decreased from 32% to 13%. Following fortification, regional variations in the prevalence and distribution of sites almost disappeared.

CONCLUSIONS:

Results confirmed the etiologic heterogeneity of spina bifida and the more pronounced effect of folic acid in decreasing the risk of the more severe clinical presentations.

MARTINEZ FRIAS ML

Bonaglia MC, Ciccone R, Gimelli G, Gimelli S, Marelli S, Verheij J, Giorda R, Grasso R, Borgatti R, Pagone F, Rodríguez L, Martinez-Frias ML, van Ravenswaaij C, Zuffardi O. **Detailed phenotype-genotype study in five patients with chromosome 6q16 deletion: narrowing the critical region for Prader-Willi-like phenotype.** Eur J Hum Genet. 2008 Jul 23. [Epub ahead of print]

1Scientific Institute E Medea, Bosisio Parini, Lecco, Italy.

Most patients with an interstitial deletion of 6q16 have Prader-Willi-like phenotype, featuring obesity, hypotonia, short hands and feet, and developmental delay. In all reported studies, the chromosome rearrangement was detected by karyotype analysis, which provides an overview of the entire genome but has limited resolution. Here we describe a detailed clinical presentation of five patients, two of whom were previously reported, with overlapping interstitial 6q16 deletions and Prader-Willi-like phenotype. Our patients share the following main features with previously reported cases: global developmental delay, hypotonia, obesity, hyperphagia, and eye/vision anomalies. All rearrangement breakpoints have been accurately defined through array-CGH at about 100 Kb resolution. We were able to narrow the shortest region of deletion overlap for the presumed gene(s) involved in the Prader-Willi-like syndrome to 4.1 Mb located at 6q16.1q16.2. Our results support the evidence that haploinsufficiency of the SIM1 gene is responsible for obesity in these patients. A possible involvement of the GRIK2 gene in autistic-like behaviour, of POPDC3 in heart development, and of MCHR2 in the control of feeding behaviour and energy metabolism is also hypothesized.

MERLOB P

Dubnov-Raz G, Juurlink DN, Fogelman R, Merlob P, Ito S, Koren G, Finkelstein Y. **Antenatal Use of Selective Serotonin-Reuptake Inhibitors and QT Interval Prolongation in Newborns.** Pediatrics. 2008 Sep;122(3):e710-5.

Hospital for Sick Children, MotheRisk Program, Divisions of Clinical Pharmacology and Toxicology and Emergency Medicine, Department of Pediatrics, 555 University Avenue Toronto, Ontario, Canada M5N2N5. yfinkel@yahoo.com.

OBJECTIVES.

Prolongation of the QT interval is a risk factor for sudden death. Selective serotonin-reuptake inhibitor antidepressants can prolong the QT interval and are widely used by pregnant women. Whether antenatal exposure to selective serotonin-reuptake inhibitor causes QT prolongation in offspring is unknown. The aim of this study was to determine the effect of maternal use of selective serotonin-reuptake inhibitor antidepressants during pregnancy on the QTc interval of the offspring.

METHODS.

Between January 2000 and December 2005, we collected data on all of the newborns born at a single tertiary care hospital. Electrocardiograms of infants exposed to selective serotonin-reuptake inhibitor antidepressants in utero were compared with those of healthy control newborns matched on gestational age. The tracings were interpreted by a pediatric cardiologist who was unaware of the drug exposure.

RESULTS.

We identified 52 newborns exposed to selective serotonin-reuptake inhibitor antidepressants in the immediate antepartum period and 52 matched control subjects. The mean QTc was significantly longer in the group of newborns exposed to antidepressants as compared with control subjects (409 +/- 42 vs 392 +/- 29 milliseconds). Five (10%) newborns exposed to selective serotonin-reuptake inhibitor antidepressants had a markedly prolonged QTc interval (>460 milliseconds) compared with none of the unexposed newborns. The longest QTc interval observed among exposed newborns was 543 milliseconds. All of the drug-associated repolarization abnormalities normalized in subsequent electrocardiographic tracings.

CONCLUSIONS.

Antepartum use of selective serotonin-reuptake inhibitor antidepressants is associated with QTc interval prolongation in exposed neonates. Additional research using a standardized protocol is needed to determine whether exposure to selective serotonin-reuptake inhibitor antidepressants in late pregnancy is also associated with arrhythmias.

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Sokolover N, Merlob P, Klinger G. **Neonatal recurrent prolonged hypothermia associated with maternal mirtazapine treatment during pregnancy.** Can J Clin Pharmacol. 2008 Summer;15(2):e188-90. Epub 2008 Jun 1.

Neonatal Intensive Care, Schneider Children's Medical Center of Israel, Petah Tiqva, Israel.

We present a case of recurrent hypothermia in concordant monozygotic twins born to a mirtazapine treated mother. The twins were born at 35 weeks gestation at birth weights of 2426 g and 2355 g. Both twins presented with recurrent hypothermia continuing until day 10 of life. Possible etiologies of hypothermia were excluded. The degree of prematurity and the weight of the twins were not consistent with prolonged thermal instability. The twins' mother was treated with mirtazapine during the entire pregnancy. Due to its serotonin and alpha 2 receptors antagonism mirtazapine is known to influence thermoregulation in adult

humans and other mammals. We suggest that maternal mirtazapine treatment during pregnancy was associated with recurrent hypothermia in both identical twins.

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Ben-Amitai D, Feinmesser M, Wielunsky E, Merlob P, Lapidoth M. **Simultaneous occurrence of anetoderma in premature identical twins.** *Isr Med Assoc J.* 2008 Jun;10(6):431-2.

Pediatric Dermatology Unit, Schneider Children's Medical Center of Israel, Petah Tikva, Israel. danb@clalit.org.il

MUTCHINIK O

Arteaga J, Luna L, Mutchinick OM. [**Diabetes, pregnancy and birth defects**]. [Article in Spanish]. *Rev Invest Clin.* 2008 Mar-Apr;60(2):107-14.

Departamento de Genética, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México, D.F.

BACKGROUND:

Diabetes mellitus affects 3 to 10% of pregnant women. The reported frequency of congenital malformations (CM) in diabetic mothers is 5.5 to 10%, contributing these defects to approximately 40% of the neonatal mortality in children of diabetic mothers (CDM). **OBJECTIVE:** To investigate the frequency and type of congenital malformations in a sample of livebirths of diabetic mothers from the Mexican population. **MATERIAL AND METHODS:**

The analyzed information was obtained from the RYVEMCE (Registro y Vigilancia Epidemiológica de Malformaciones Congénitas). We analysed the type and frequency of the different CM diagnosed. These frequencies were compared with the whole amount of those CM included in the database of our registry (20,381). As part of the analysis, other maternal and neonatal variables were also compared between CDM and the control group.

RESULTS:

A total of 314 CDM (0.77%), 234 malformed and 80 non malformed were identified. The frequencies of cleft palate (CP), limb reduction defect (LRD) and microcephaly (MIC) were significantly higher in CDM than in the rest of malformed newborns of not diabetic mothers of the RYVEMCE (OR: 9.9, 3.8 and 10.0, respectively). A higher frequency of macrosomia was observed in CDM (18.0%) than in controls (6.1%), OR: 3.4, $p < 0.001$, in the frequency of preterm birth (28.5% than controls 13.0%), OR: 3.02, $p < 0.0001$ and in caesarean delivery (71.5% than controls 44.4%) OR: 3.15, $p < 0.00001$.

CONCLUSIONS:

Our results confirm the higher frequency of CM in CDM and in particular a higher risk for CP, LRD and MIC. Pregnancy and delivery complications such as macrosomia and preterm and caesarean delivery were also more frequent in CDM than controls. Certain associations of CM not described previously, were observed in the studied sample. Our results confirm the need of pregnancy planning including a pre-gestational and gestational control of maternal glycaemia, particularly in a population with such a high prevalence of diabetes mellitus as the observed in the Mexican one.

SCARANO G

Fazzo L, Belli S, Minichilli F, Mitis F, Santoro M, Martina L, Pizzuti R, Comba P, Martuzzi M, Bianchi F; Working Group. Collaborators: Bertollini R, Martuzzi M, Mitis F, Bellino M, Carboni C, Comba P, Cossa L, De Nardo P, Falleni F, Fazzo L, Musmeci L, Piccardi A, Trinca S, Bianchi F, Linzalone N, Minichilli F, Pierini A, Lorenzo E, Martina L, Pizzuti R, Santoro M, Lionetti E, Menegozzo M, Fusco M, Scarano G, Menegozzo S, Menegozzo S, Doddi G, Leonardi M, Madeo L, Martini G, Matteucci M, Mazzei N, Pizzi R, Savarese A, Bove C, D'Argenzio A, Simonetti A, Parlato A, Peluso F, Palombino R, Giugliano F. **Cluster analysis of mortality and malformations in the Provinces of Naples and Caserta (Campania Region)**. Ann Ist Super Sanita. 2008;44(1):99-111.

Dipartimento Ambiente e Connessa Prevenzione Primaria, Istituto Superiore di Sanità, Rome, Italy. lucia.fazzo@iss.it

The possible adverse health effects associated with the residence in the neighbourhood of toxic dump sites have been the object of many epidemiological studies in the last two decades; some of these reported increases of various health outcomes. The present study reports the cluster analysis of mortality and malformations at municipality level, standardized by socioeconomic deprivation index, in an area of the Campania Region characterized by a widespread illegal practice of dumping toxic and urban waste. Clusters have been observed with significant excess of mortality by lung, liver, gastric, kidney and bladder cancers and of prevalence of total malformations and malformations of limb, cardiovascular and urogenital system. The clusters are concentrated in a sub-area where most of the illegal practice of dumping toxic waste has taken place

SIPEK A

Gregor V, Sípek A, Horáček J, Sípek A Jr, Langhammer P. **[The analysis of incidence of selected types of birth defects in the Czech Republic according to a multiplicity of pregnancy]**. [Article in Czech]. Ceska Gynekol. 2008 Jul;73(4):199-208.

Oddělení lékařské genetiky, Fakultní Thomayerova nemocnice, Praha. vladimir.gregor@ftn.cz

OBJECTIVE:

To analyze an occurrence of selected types of birth defects in single and multiple pregnancies in the Czech Republic in 1994-2006 period.

DESIGN:

A retrospective epidemiological analysis of birth defects according to a multiplicity of pregnancy.

SETTING:

Department of Medical Genetics, Thomayer's University Hospital, Prague. Chair of Medical Genetics, Postgraduate Medical Institute, Prague.

METHODS:

Data were collected from National Birth Defects Register (Institute of Health Information and Statistics). Incidences of selected types of birth defects according to pregnancy multiplicity were analyzed.

RESULTS:

In 1994-2006, totally 1 132 567 children were born in the Czech Republic, out of which more than 42 000 with a birth defect. In all particular defects, incidences were increased in children born from multiple pregnancies compared to singletons.

CONCLUSION: Highest differences in birth defects incidences in children born from single versus multiple pregnancies were found in neural tube defects group and in congenital hydrocephalus.

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Gregor V, Sípek A, Horáček J, Sípek A Jr, Langhammer P. [**Prenatal diagnostics of selected types of birth defects in the Czech Republic in 1994 - 2006 period**]. [Article in Czech]. Ceska Gynekol. 2008 Jun;73(3):169-78.

Oddělení lékařské genetiky, Fakultní Thomayerova nemocnice, Praha.
vladimir.gregor@ftn.cz

OBJECTIVE:

To analyze an efficiency of prenatal diagnostics of selected types of birth defects in the Czech Republic in 1994 - 2006 period.

DESIGN:

A retrospective epidemiological study and a prenatal diagnostics efficiency analysis.

SETTING:

Department of Medical Genetics, Thomayer's University Hospital, Prague. Chair of Medical Genetics, Postgraduate Medical Institute, Prague, Czech Republic.

METHODS:

Data were collected from National Birth Defects Register (Institute of Health Information and Statistics). Incidences of selected types of birth defects were analyzed.

RESULTS:

In 1994 - 2006, totally 1 132 567 children were born in the Czech Republic, out of which more than 42 000 with a birth defect. A mean incidence was 339 per 10 000

live births with a maximum of 414.58 per 10 000 in 2003. In the same time period, 6113 cases of birth defect prenatal diagnostics (493 per 10 000 live births) were reported.

CONCLUSION:

In a comparison of 1980 - 1993 and 1994 - 2006 periods, a significant increase of prenatal diagnostics efficiency was recorded.

Gregor V, Sípek A, Horáček J, Sípek A Jr, Langhammer P. [**Survival in children with birth defects during first year of their life**]. [Article in Czech]. Ceska Gynekol. 2008 Jun;73(3):163-9.

Oddělení lékařské genetiky, Fakultní Thomayerova nemocnice, Praha.
vladimir.gregor@ftn.cz

OBJECTIVE:

To analyze infant mortality in children with selected types of birth defects during a first year of their life. **DESIGN:**

A retrospective study with an analysis of prenatal and postnatal occurrence of birth defects in the Czech Republic during 1994 - 2006.

SETTING:

Department of Medical Genetics, Thomayer's University Hospital, Prague. Chair of Medical Genetics, Postgraduate Medical Institute, Prague.

METHODS:

Data were collected from national registers (Institute of Health Information and Statistics) and particular departments of medical genetics. A study of frequency of 14 selected birth defects was performed along with an analysis of survival and mortality in children with birth defects during a first year of their life.

RESULTS:

In 1994 - 2006, totally 1 132 567 children were born in the Czech Republic, out of which more than 42 000 with a birth defect. A mean incidence was 339 per 10 000 live births with a maximum of 41458 per 10 000 in 2003. In correctible defects, first year survival was lowest in congenital hydrocephalus (72%) and neural tube defects (anencephaly excluded) (71%). In congenital defects of gastro-intestinal tract and in abdominal wall defects survival was between 82-91%.

CONCLUSION:

Birth defects present an important contribution to an infant mortality and morbidity in the first year of life. In a comparison of 1980 - 1993 and 1994 - 2006 periods, a significant increase of prenatal diagnostics efficiency was recorded.

SULLIVAN E

Cliffe SJ, Tabrizi S, Sullivan EA; Pacific Islands Second Generation HIV Surveillance Group. Collaborators: Ali ST, Raikuna L, Robate M, Toatu T, Vaai SA, Pasa-Anesone E, Paulsen J, Puiahi E, Kupu S, Penitani S, Laklotal M, Phatu T, Tabrizi S, Sladden T, Black D, Cliffe S, Dean J, Maher L, Sullivan E, Wang YA, Danielsson N, Faasino A, Hii J, Seya R, Sopheap S, Thuy NT. **Chlamydia in the Pacific region, the silent epidemic.** Sex Transm Dis. 2008 Sep;35(9):801-6.

Perinatal and Reproductive Epidemiology and Research Unit, School Women's and Children's Health, University of New South Wales, Randwick, New South Wales, Australia.

BACKGROUND:

Second generation surveillance of HIV infection and sexually transmitted infections (STIs) among pregnant women in 6 Pacific Island Countries and Territories were undertaken to improve knowledge and to make recommendations on future prevention and management of STIs.

METHODS:

Cross-sectional studies, using standardized questionnaire, laboratory tests, and protocols were undertaken in Fiji, Kiribati, Samoa, Solomon Islands, Tonga, and Vanuatu between 2004 and 2005. For each country, between 200 and 350 pregnant women aged 15 to 44 years were consecutively recruited from antenatal clinics located in the main hospital of the major urban centre of each Pacific Island Countries and Territories. Consenting participants were interviewed about their socio-demographic characteristics and their sexual behavior, and were tested for HIV, chlamydia, syphilis (*Treponema pallidum* antibody seroactivity), and gonorrhoea.

RESULTS:

Amongst the 1618 pregnant women studied, the most prevalent STI was Chlamydia with 26.1% of women under 25 and 11.9% of women aged 25 years and over being positive. Highest infection was detected in single teenage women with 38.1% positive for chlamydia. The overall prevalence of gonorrhoea and syphilis was 1.7% and 3.4%, respectively. No case of HIV was detected. Chlamydia infection was independently associated with younger age, being nulliparous, single status, multiple lifetime sexual partners, and commercial sex activity.

CONCLUSION:

In a population of young women, chlamydia infection was endemic. Regional leadership is needed to implement strategies to prevent the spread of chlamydia and to implement HIV and STI prevention and management.

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Cliffe S, Black D, Bryant J, Sullivan E. **Maternal deaths in New South Wales, Australia: a data linkage project.** Aust N Z J Obstet Gynaecol. 2008 Jun;48(3):255-60.

National Perinatal Statistics Unit, School Women's and Children's Health, University of New South Wales, New South Wales, Australia.

BACKGROUND:

The magnitude of maternal mortality is underestimated as deaths occurring beyond the traditional 42-day time period after the pregnancy ending ('late death') have not been reported routinely in Australia. Aims: The aims of this study were to undertake a data linkage study to improve the ascertainment of maternal deaths and to determine the number of deaths occurring 43-365 days after the pregnancy ended ('late maternal death').

METHODS:

Data from the New South Wales Midwives Data Collection were linked with the Australian Institute of Health and Welfare National Death Index. Australian identified pregnancy-related deaths were then coded as direct, indirect and incidental to the pregnancy.

RESULTS:

During the period 1994-2001, 173 maternal deaths were identified. Of these, 97 were classified as occurring up to 42 days of the pregnancy ending, 15 (15.5%) of which were previously unknown to the maternal mortality committee. In addition, 76 deaths were classified as occurring between 43 and 365 days after the pregnancy ended. The majority (70 of 76) of these late deaths were only identified through the linkage study. Most (73 of 76) of these deaths were classified as indirect maternal deaths with the most common causes of deaths suicide (n= 23), cardiac disorders (n= 16) or accident/violence (n= 16).

CONCLUSIONS:

The ascertainment of maternal and late maternal mortality was enhanced through data linkage of birth and mortality data. Data linkage is a viable method for monitoring late maternal deaths.

TENCONI R

Clementi M, Tiboni GM, Causin R, La Rocca C, Maranghi F, Raffagnato F, Tenconi R. **Pesticides and fertility: An epidemiological study in Northeast Italy and review of the literature.** *Reprod Toxicol.* 2008 Sep;26(1):13-8. Epub 2008 Jul 3.

North East Registry of Congenital Malformations, Genetica Clinica ed Epidemiologica, Dipartimento Pediatria, Università di Padova, Italy.

An increasing number of observations suggestive for a causal link between pesticide exposure and reproductive dysfunctions have appeared in literature during recent years. The present epidemiological analysis was undertaken to evaluate whether living in rural areas, where large amounts of pesticides are applied, represents a risk factor for infertility. Fertility rate (FR) was taken as statistical indicator for potential changes in fertility mediated by pesticides. The study analyzed a large population from an agricultural area of

the North Eastern Italy, the Veneto Region. According to the estimated quantities of sprayed pesticides, the area was divided in three sub-areas with expected low, intermediate and high pesticide exposure. Comparisons of FR failed to detect significant differences among populations from the three selected areas, while regression analysis showed a significant decrease of FR relative to the total amount of pesticides used. Although several investigative shortcomings prevent the results from being conclusive, this study seemingly challenges the hypothesis that living in rural areas where large amounts of pesticides are applied represents a risk factor for fertility.

VOLLSET SE

Nilsen RM, Vollset SE, Rasmussen SA, Ueland PM, Daltveit AK. **Folic acid and multivitamin supplement use and risk of placental abruption: a population-based registry study.** Am J Epidemiol. 2008 Apr 1;167(7):867-74. Epub 2008 Jan 10.

Section for Epidemiology and Medical Statistics, Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway. roy.nilsen@uib.no

The authors investigated a possible association of supplemental folic acid and multivitamin use with placental abruption by using data on 280,127 singleton deliveries recorded in 1999-2004 in the population-based Medical Birth Registry of Norway. Odds ratios, adjusted for maternal age, marital status, parity, smoking, pregestational diabetes, and chronic hypertension, were estimated with generalized estimating equations for logistic regression models. Use of folic acid and/or multivitamin supplements before or any time during pregnancy was reported for 36.4% of the abruptions (0.38% of deliveries) and 44.4% of the nonabruptions. Compared with no use, any supplement use was associated with a 26% risk reduction of placental abruption (adjusted odds ratio = 0.74, 95% confidence interval: 0.65, 0.84). Women who had taken folic acid alone had an adjusted odds ratio of 0.81 (95% confidence interval: 0.68, 0.98) for abruption, whereas multivitamin users had an adjusted odds ratio of 0.72 (95% confidence interval: 0.57, 0.91), relative to supplement nonusers. The strongest risk reduction was found for those who had taken both folic acid and multivitamin supplements (adjusted odds ratio = 0.68, 95% confidence interval: 0.56, 0.83). These data suggest that folic acid and other vitamin supplementation during pregnancy may be associated with reduced risk of placental abruption.

ZHU LI

Hao L, Yang QH, Li Z, Bailey LB, Zhu JH, Hu DJ, Zhang BL, Erickson JD, Zhang L, Gindler J, Li S, Berry RJ. **Folate status and homocysteine response to folic acid doses and withdrawal among young Chinese women in a large-scale randomized double-blind trial.** Am J Clin Nutr. 2008 Aug;88(2):448-57.

National Reference Laboratory on Reproductive and Child Health, Ministry of Health and National Center for Maternal and Infant Health, Peking University Health Science Center, Beijing, China.

BACKGROUND:

There are no large randomized trials of the effect of folic acid dosing regimens on blood folate and homocysteine concentrations.

OBJECTIVE:

We aimed to evaluate the changes in folate and homocysteine concentrations in response to different folic acid doses and to withdrawal in young women not exposed to other sources of folic acid.

DESIGN:

Women (n = 1108) were randomly assigned to 1 of 6 intervention groups for which daily intakes of folic acid for 6 mo were 100 microg 1 time/d, 25 microg 4 times/d, 400 microg 1 time/d, 100 microg 4 times/d, 4000 microg 1 time/d, or 4000 microg 1 time/wk. Plasma and red blood cell folate and homocysteine concentrations were measured at baseline; at 1, 3, and 6 mo; and 3 mo after the discontinuation of folic acid. **RESULTS:**

Folate and homocysteine concentrations were not different at baseline between the groups who had the same daily intake of folic acid as a single dose or multiple doses (P = 0.058). Plasma folate concentrations plateaued at 3 mo with 108% (95% CI: 97.7%, 120%), 259% (95% CI: 240%, 279%), 460% (95% CI: 417%, 503%), and 142% (95% CI: 123%, 162%) observed increases for the folic acid groups receiving 100, 400, and 4000 microg/d and 4000 microg/wk, respectively. The rate of reduction in folate concentrations during the 3 mo after cessation of folic acid was dose-dependent—higher intakes were associated with faster reductions.

CONCLUSIONS:

Changes in folate and homocysteine concentrations were unaffected by different dosing schedules. After folic acid cessation, blood folate declined rapidly, which indicated that the intervention-enhanced folate status was rapidly diminished.