

However, an increased risk for preeclampsia may be related to maternal use of adrenergic drugs, and gestational diabetes to maternal use of corticosteroids. An increased risk for orofacial clefts was not related to corticosteroid use and may be spurious or related to the underlying disease.

#### 250. In-Utero Exposure to Antihistamines and the Risk of Congenital Hypospadias or Cryptorchidism in Male Births (240)

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**Background:** Hypospadias and cryptorchidism are congenital abnormalities in newborn infants that are purportedly aetiologically linked. A recent study using Swedish registry data showed an association between a non-sedating antihistamine exposure in early pregnancy and hypospadias.

**Objective:** To test the hypothesis that in-utero exposure to sedating and non-sedating antihistamines is associated with hypospadias or cryptorchidism.

**Methods:** A case control study design was used within the cohort of all mother baby pairs within the Full Feature General Practice Research Database (FF-GPRD). The mother-baby cohort was created by linking births with deliveries using family identifiers and aligning delivery and birth dates. Case and control eligibility criteria included full maternal pregnancy records with the child registered by the age of six months for six months or longer. Cases were identified as infants born between 1990 and 2002 with a record of hypospadias or cryptorchidism. Four controls were matched per case by practice, maternal age and delivery year. Exposure information was defined by the prescription of a sedating or non-sedating antihistamine (SAH or NSAH). Potential confounders included gestational age, sex hormones, diabetes, maternal age and smoking.

**Statistical Analysis:** Matched conditional logistic regression analysis was performed to estimate adjusted odds ratios (ORs) accounting for potential confounders.

**Results:** Overall there were 545 hypospadias and 2159 cryptorchidism cases; 16 cases had both conditions. Exposure during pregnancy to SAH was found in 3.9% (105) cases and 3.8% (407) controls and to NSAH in 1.7% (46) cases and 1.8% (186) controls. There was no association between NSAH use during the first trimester of pregnancy and hypospadias or cryptorchidism [Adjusted OR = 1.00 (0.50, 1.25)]. Overall, antihistamine use during pregnancy was not associated with hypospadias or cryptorchidism for either drug class [SAH: OR = 0.96 (0.71, 1.28), NSAH: OR = 0.78 (0.50, 1.24)].

**Conclusion:** This study provides no evidence of an increased risk of hypospadias or cryptorchidism following exposure to antihistamines during early pregnancy. Although these conditions are aetiologically linked, further analyses are needed to investigate the relationship between NSAH use and hypospadias and cryptorchidism separately.

#### 251. Pregnancy Outcome Following Early Gestational Exposure to Leflunomide: The Otis Rheumatoid Arthritis in Pregnancy Study (104)

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**Background:** Based on reproductive toxicity studies in animals, female patients who take leflunomide are advised not to become pregnant. However, there is insufficient published human data supporting or refuting the teratogenic potential of this medication.

**Objective:** The Organization of Teratology Information Services (OTIS) has established the Rheumatoid Arthritis (RA) in Pregnancy Study to evaluate the safety of leflunomide when used early in pregnancy.

**Methods:** Women who contact one of 25 OTIS member services in North America are the primary source of subjects. A controlled cohort study design is used, with subjects prospectively enrolled early in pregnancy in one of three groups 1) women with RA who have used leflunomide early in pregnancy, 2) women with RA who have not used leflunomide, and 3) women who do not have RA. All women are followed with repeated structured interviews and data are abstracted from medical records. All live born children receive a standardized, blinded physical examination by one of three study dysmorphologists within six months after delivery. Main outcome measures include the birth prevalence of major and minor structural defects, preterm delivery, and prenatal growth deficiency. Comparisons are made using standard univariate techniques, logistic regression, and ANCOVA.

**Results:** As of January, 2004, pregnancy outcome has been documented on 168 subjects (43 leflunomide-exposed, 78 RA controls, and 47 non-diseased controls). The proportion of infants born with major and/or minor malformations was similar between groups. Both the leflunomide-exposed and the RA controls were significantly more likely to deliver preterm infants relative to non-diseased controls (leflunomide group: adjusted odds ratio 12.0, 95% CI 2.5, 59.2; RA control group: adjusted odds ratio 10.1, 95% CI 2.2, 47.3). Mean birth weight of full term infants in both RA groups was also significantly lower than that in non-diseased controls (leflunomide group: adjusted mean 3158 gms, 95% CI 2979, 3336; RA control group: adjusted mean 3250 gms, 95% CI 3124, 3375; non-diseased control group: adjusted mean 3618 gms, 95% CI 3487, 3748;  $p < 0.001$ ).

**Conclusion:** Further analysis at completion of this study is necessary to rule out a more subtle pattern of effect on embryonic development. However, preliminary findings suggest that the increased risks for preterm delivery and growth deficiency among infants born to mothers with RA are reasonably attributed to the maternal underlying disease or possibly concomitant use of other medications such as corticosteroids to treat RA.

### 252. Positive Predictive Value of Computerized Databases for Birth Defects in a Medicaid Population (453)

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**Background:** Birth defect surveillance is important for monitoring incidence over time and for detecting potentially teratogenic effects of prescription drugs during pregnancy. Assessing the positive predictive value of computerized data sources in a population with large numbers of minorities and persons with chronic health conditions such as Medicaid would provide important information about birth defects in this traditionally understudied population.

**Objective:** To assess the positive predictive value of computerized vital records and Medicaid claims to detect birth defects in a Medicaid population.

**Methods:** A retrospective cohort study included 37 527 mother/infant pairs assembled for a study of prenatal antibiotic exposure in which the mother and infant were enrolled in Medicaid in a single state throughout pregnancy and following delivery, 1985–2000. Birth defects were identified from birth certificates (BC's) (text fields pre-1989, check-boxes 1989+), death certificates (DC's) (ICD-9 or ICD-10 codes), Medicaid claims (ICD-9 codes). Possible birth defects identified in computer databases were confirmed through review of medical records for hospitalizations through the first year of life. Medical record confirmation required either physical exam, radiological, surgical, or autopsy evidence, depending on the birth defect. Validation records were reviewed for a random sample of children without computerized evidence of birth defects. Positive predictive value (PPV) was calculated using the medical record as the gold standard for all sources combined, claims, and birth certificates. The small number of DC defects precluded calculation of PPV for this source.

**Results:** Among 1459 possible birth defects identified from combined sources, 786 were confirmed (PPV = 53.9%); claims PPV = 64.8%, BC's = 42.9%. For cardiac defects, confirmation of 318/454 possible defects for all sources yielded a PPV = 70.0%; claims = 78.8%, BC's = 54.5%. For gastrointestinal defects, confirmation of 111/153 possible defects yielded a PPV = 72.5%; claims = 73.6%, BC's = 83.3%. For genitourinary defects, confirmation of

141/193 possible defects yielded PPV = 73.0%; claims = 79.6%, BC's = 66.7%. Specific defects had better PPV: VSD = 89.3% all sources, hypospadias = 93.4%, cleft palate = 97.0%, pyloric stenosis = 89.5%. Among validation records without evidence of a birth defect in the data sources, 285/286 (99.7%) were confirmed to not have a birth defect in the medical record.

**Conclusion:** Depending on the defect, computerized data sources offer opportunities for identifying birth defects in populations of vulnerable persons.

### 253. Development of a Surveillance and Signal Detection System To Monitor Medication Exposure during Pregnancy and Lactation (233)

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**Background:** On-going surveillance of gestational exposure to drugs can be a very useful tool to monitor new products recently put on the market or old drugs with new indications.

**Objective:** To develop a surveillance and signal detection system to study prevalence, patterns and trends of drug utilisation during pregnancy and lactation using a computerized database generated from calls to a teratology information service.

**Methods:** Using the computerized database of IMAGe, a teratology information service, a surveillance and signal detection system was developed using time-series modelling. IMAGe (Info-Médicaments en Allaitement et Grossesse) provides evidence-based data regarding medication use during pregnancy and lactation over the telephone for the population of Quebec. On 12/01/2003, a research infrastructure was put in place to allow real-time entry of all data collected at IMAGe. After every call, data are now automatically downloaded in a database which constitutes the first computerized teratology information service database. This database is the backbone for the surveillance and signal detection system. The surveillance and signal detection system was developed using SQL Server and provides descriptive statistics and graphics on the utilisation of medications during pregnancy and lactation; categorization of medications is made using Health Canada medication library and MedDRA is used for disease classification. The system can also be linked to the RAMQ database for ascertainment of pregnancy outcomes. ARIMA time-series models were incorporated in the system to detect abnormal signals on an annual basis. The system is further capable of detecting year-to-year variations in frequencies of medication use.

**Results:** IMAGe received 1815 calls between 12/01/2003 and 02/15/2004. The most prevalent medication classes used during pregnancy were antidepressants (16%), NSAIDs