#### Society for Pediatric and Perinatal Epidemiologic Research

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#### History of weight cycling and weight changes during and after pregnancy

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We examined whether a history of weight cycling was associated with prenatal weight gain and postpartum weight retention (relative to pregravid weight) in 549 white women in a US military population. We measured postpartum weights and obtained other data from questionnaires and prenatal records for mothers of infants receiving well-baby care at the Naval Medical Center, San Diego between 1997 and 1999. Women with a history of dieting off and regaining >10 lb at least twice were classified as weight cyclers. Compared with non-cyclers, cyclers had significantly higher pregravid BMIs and postpartum weight retention (5.1 kg, standard deviation (sd) = 8.1 vs. 3.6 kg, sd = 5.8) but similar prenatal gains of about 16 kg. Separate multiple linear regression models (adjusting for pregravid weight, height and sociodemographic variables) suggested that weight cycling was related to both gestational weight gain and to postpartum weight retention (mean time = 311 days after birth). Since there was evidence that pregravid BMI modified these relationships, we stratified the data by BMI (<26 vs. >26). After adjusting for covariates and gestational age, non-overweight cyclers gained more weight during pregnancy (regression coefficient,  $\beta = 1.61$ kg, standard error (se) = 0.56, p < 0.01). After adjusting for covariates, gestational gain and time since delivery, non-overweight cyclers retained more weight late in the postpartum year  $(\beta = 1.43 \text{ kg}, \text{ se} = 0.66, \text{ p} = 0.03)$  than non-cyclers. In contrast, weight cycling was not significantly associated with either gestational gain or postpartum weight retention in women who were overweight before pregnancy.

#### Weight cycling, ethnicity, and postpartum weight retention

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Research suggests that weight cycling is associated with difficulty losing or maintaining weight and thus may be a risk marker that will presage overweight/obesity. Most women retain weight after pregnancy but it is uncertain if a history of weight cycling influences weight retention 6–24 months after delivery (mean = 321

days, standard deviation = 79). The literature also suggests an ethnic difference in the amount of retained weight. The study group included new mothers whose infants received well-baby care at the Naval Medical Center, San Diego from 1997 to 1999. Women were categorized as never losers (n = 441), weight loss maintainers (n = 217), or cyclers (n = 702); data were analyzed by multivariable linear regression. After adjusting for 8 covariates and time since birth, cycling was significantly associated with increased weight retention (multiple regression coefficient = 1.9 kg (standard error [se] = 0.44, p < 0.01) compared with the other groups. There were 813 White, 177 Black, 152 Asian, and 218 Hispanic mothers. Prevalence (%) of weight cycling was 53.4, 46.3, 46.7, and 52.8, and mean postpartum weight retention was 4.2 kg, 4.0 kg, 3.6 kg, and 4.6 kg in each of these groups, respectively. After adjustment, the multiple regression coefficients for weight cycling were 1.7 kg (se = 0.58, p = 0.003) for Whites, 3.3 kg (se = 1.4, p = 0.02) for Blacks, 1.8 kg (se = 0.97, p = 0.07) for Asians, and 1.1 kg (se = 1.2, p = 0.33) for Hispanics. Thus, weight cycling appears to be a risk factor for increased postpartum weight retention but ethnic factors, possibly behavioral in nature, do seem to modify this relationship.

#### Childhood asthma prevalence: the impact of the 1997 National Health Interview Survey redesign

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Background. Estimates of US childhood asthma prevalence were affected by the 1997 National Health Interview Survey (NHIS) redesign. In 1997, only 5.5% of children were estimated to have asthma compared with 7.5% in 1995. The contribution of the survey redesign to this reported decline is unknown. Objective. To examine the impact of the NHIS 1997 redesign on childhood asthma prevalence estimates. Methods. In 1988, 50% of children from the core NHIS participated in a Child Health Supplement (CHS). The CHS questions differ from those in the core NHIS and are similar to the new asthma questions used in the 1997 NHIS. First, childhood asthma prevalence estimates from the 1988 core NHIS and the CHS were directly compared. A second comparison was limited to the sample participating in both the core NHIS and the CHS. For this sample, the percent difference between core NHIS and CHS estimates was calculated for 6 race/age strata (black and white, ages 0-4, 5-10, and 11-17 years). The 1997 estimates for each stratum were adjusted by these differences, and a new adjusted 1997 estimate was produced using the 1997 population distribution for each stratum. **Results.** The first method resulted in an 18.6% difference between asthma prevalence estimates from the 1988 core NHIS and CHS (5.1% vs. 4.3%). Simply inflating the 1997 asthma prevalence estimate of 5.5% by 18.6% yielded an adjusted estimate of 6.5%. The second stratification method produced an adjusted 1997 asthma prevalence estimate of 7.3%. **Conclusion.** The redesigned NHIS likely produces lower asthma prevalence estimates than the previous NHIS. Adjusting the 1997 estimate to compensate for the redesign suggests that childhood asthma prevalence has plateaued since 1995, not declined.

#### Secular trends in singleton small-for-gestationalage births in blacks and whites in the US

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Objective. To evaluate secular trends in singleton preterm (28–36 weeks) and term (37-41 weeks) small-for-gestational-age (SGA) births, and to estimate the relative contributions of potential determinants of SGA births, separately among blacks and whites. Design. The authors performed a population-based, cohort study comprising blacks (n = 1084 935) and whites (n = 5403 858) that delivered singleton live births in the US in 1989 and 1998. Changes in rates of SGA births (defined as sex-specific birthweight below the 10th centile for gestational age, based on 1989 US births) before and after adjustment for demographic, behavioral determinants and medical and obstetrical complications of current pregnancy. Results. Preterm SGA birth rates among whites increased from 8.5% in 1989 to 9.3% in 1998, a relative increase of 9.4%. Comparable rates among blacks for 1989 and 1998 were 10.5% and 12.4%, respectively, a relative increase of 18.5%. Among term births, the SGA rates declined by 8.1% in whites (9.8% in 1989 and 9.0% in 1998) and by 11.0% among blacks (19.5% in 1989 and 17.3% in 1998). When sequentially adjusted for potential determinants by multivariable logistic regression, the increase in preterm SGA rates were partly explained by pregnancy-induced hypertension and, to a lesser extent, by unmarried status. None of the potential determinants, however, significantly accounted for the decline in term SGA rates. Conclusions. A secular increase in the rate of preterm SGA births in the US and a decline among term SGA births was apparent. These results underscore how little is known about the causes of the observed trends. The importance of these trends on the risks of fetal and neonatal mortality also remains largely unexplored.

#### The effect of overweight and race on age of menarche in a representative survey of US girls

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Despite widespread belief in a trend toward earlier ages at menarche in the US, it is unclear if the evidence justifies speculation

about possible environmental causes of early puberty. Previous studies were not representative of the US population and did not account for body weight, a known factor in maturational timing. The authors examined the relationship between weight, race, and menarcheal status in girls ages 11-14 in the National Health and Nutrition Examination Survey III (1988-94) and compared the results to the National Health Examination Survey (1963-70) where the median age at menarche was 12.8 years. A logit model was used to calculate median age at menarche, overall and by race, based on the weighted proportions of girls who were menarcheal at each age. The median age at menarche in NHANES III was 12.6 (95% confidence interval [CI]: 12.0, 13.1), 12.1 (95%CI: 11.9, 12.3) for Blacks, and 12.7 (95%CI: 11.7, 13.5) for Whites. The prevalence of overweight, defined as a body mass index (BMI) above the 85th percentile based on the CDC growth charts, was 29.9% overall, 29.3% for Whites, and 35.6% for Blacks. High BMI was associated with earlier age at menarche. The median age at menarche for girls with a BMI above the 85th percentile was 12.2 years (95%CI: 11.0, 13.0), and was 12.7 years (95%CI: 12.2, 13.2) for girls with a BMI below the 85th percentile. In a multiple logistic regression model using SUDAAN, overweight and Black race were independently associated with increased likelihood of reaching menarche at a given age: OR = 2.3 (95%CI: 1.3, 4.0) overweight; OR = 2.3 (95%CI: 1.2, 4.4) Black. There was no evidence for a race by overweight interaction (P = 0.41). These findings suggest that any decrease in age at menarche in the US is likely due to the increased prevalence of childhood obesity.

#### Adverse outcomes in pregnancies complicated by early vaginal bleeding

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Objectives. To assess the perinatal risk of deliveries complicated by light and heavy bleeding, trying to predict the high-risk pregnancies. To evaluate the association between bleeding and perinatal complications in the presence of other confounders. Methods. A case-control, hospital-based study was conducted in the two major obstetric hospitals in Alexandria where women were interviewed during their postpartum stay through 1998. A total of 1503 singleton deliveries, of whom 159 (10.6%) reported bleeding, 101 (63.5%) during the first trimester and 58 (36.5%) during the second. The remaining 1344 women served as controls. Initially, contingency  $\chi^2$  tests were used to explore the association between bleeding and outcomes, then logistic regression models were used to control for other confounders. Results. Bleeding was more frequent in women of more advanced age (>33 years), with a history of LBW, previous miscarriage and low social class. Suboptimal outcomes (LBW, preterm deliveries, perinatal death and SGA) occurred more often in women reporting bleeding than in those who never bled, and the risk was significantly increased with second trimester bleeding after control for confounders. Logistic regression revealed an interaction among bleeding, interpregnancy interval, and outcomes in that the risk of LBW, preterm, and neonatal death were significantly decreased when the interval was taken into consideration. Con**clusion.** Early bleeding indicates a poor pregnancy outcome, especially during the second trimester, and the risk of LBW, preterm, and neonatal death decreased with increasing pregnancy interval.

#### Unexamined deaths: perinatal mortality in the United States, 1995–97

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Background. Infant mortality (death < 1 years of age) is used to gauge a nation's quality of health care and socioeconomic conditions, but it excludes late fetal deaths that might be etiologically similar to early neonatal deaths. Surveillance of perinatal mortality (late fetal plus early neonatal deaths) is needed to provide a complete picture of the health of women, fetuses, and newborns. Methods. Fetal Death and Linked Birth/Infant Death data sets were analyzed for 1995–97. Perinatal mortality rates (per 1000 live births and fetal deaths) and rate ratios between blacks and whites were calculated. Components of perinatal mortality - late fetal deaths (>28 weeks' gestation) and early neonatal deaths (<7 days of age) - were compared within races. Late neonatal (7-27 days of age) and postneonatal (28-364 days of age) deaths were also determined. Results. During 1995–97, the total perinatal mortality rate was 7.6. More perinatal deaths (85 465) occurred than late neonatal (10 992) or postneonatal (29 643) deaths; 47% of perinatal deaths were fetal deaths, and >50% of fetal deaths occurred at 36-41 weeks' gestation. Blacks had higher perinatal mortality rates than whites (rate ratio = 2.1). Among perinatal deaths at >28 weeks' gestation, the ratio of fetal to neonatal deaths was 3.4 for blacks and 2.4 for whites. Conclusions. Most fetal and infant deaths occur during the perinatal period; many occur among older, potentially viable fetuses. Late fetal deaths might be more common among blacks because of increased adverse outcomes late in pregnancy; reporting of fetal vs. neonatal deaths might account for some differences. Perinatal mortality surveillance helps to target interventions to prevent deaths among viable fetuses and reduce racial disparities.

## Results of a reproductive age mortality survey (RAMOS) among Afghan refugee women in Pakistan, 1999–2000

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Reproductive health (RH) status, largely undocumented in refugee settings, is needed to guide resource allocation, plan

health care services and develop policy related to RH. This report presents results from a reproductive age mortality survey (RAMOS) conducted among Afghan refugees in Pakistan to determine the magnitude of mortality due to RH-related causes and identify preventable factors for program intervention. RH-related deaths include those related to pregnancy or delivery; or reproductive tract infections (RTI) including HIV. Deaths among males and females of all ages between January 20, 1999 and August 31, 2000 were identified in a census of all families living in 12 refugee villages in Hangu, Pakistan (population = 134406). All deaths among women of reproductive age were further investigated by verbal autopsy interviews of family members to determine cause of death; whether it was RH-related, and whether there were barriers to health care access and potential for prevention. Overall, 1195 deaths occurred during the study period, 66 among women of reproductive age (15–49 years). Of the 66 deaths, 28 (41%) were related to pregnancy or complications; no deaths were related to RTI. The maternal mortality ratio was 291/100 000 live births. Of the women who died of RH-related causes, 64% were judged to be preventable, vs. 24% of women who died of non-RH-related causes (P = 0.001). Program interventions are being developed to address health care barriers including increasing the number and training of birth attendants; and improving access to emergency transportation and obstetric services.

### Pregnancy-related mortality in the United States, 1991–97 – the gaps persist

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Pregnancy-related mortality is a key public health indicator. Higher risks of death due to pregnancy and its complications occur among certain groups of women, including black women and older women. The authors examined factors associated with these deaths. Data for 1991-97 from the CDC's ongoing Pregnancy Mortality Surveillance System were analyzed. Pregnancyrelated death was defined as the death of a woman during or within one year of pregnancy caused by pregnancy, its treatment or complications. Pregnancy-related mortality ratio (PRMR) was defined as the number of pregnancy-related deaths per 100 000 livebirths. The overall PRMR was 11.5; it varied from 10.4 in 1991 to 13.0 in 1997. The PRMR was 29.5 for black women and 7.9 for white women. The ratio of the PRMR for black women compared with white women was 3.7. Mortality varied with maternal age; compared with women 15 to 19 years, who had the lowest PRMR (8.6), women > 39 years a PRMR of 44.4. Embolism was the leading cause of death, followed by hemorrhage and hypertensive disorders. Almost 90% of deaths occurred after 20 weeks' gestation; 68% followed a livebirth. Forty-five percent occurred before delivery or within the first 24 h postpartum; 85% occurred within 42 days of delivery - the traditional definition of maternal mortality. The average PRMR for 1991-97 was 30% higher than in 1990, most likely due to use of computer linkage to identify these deaths. The excess risk of pregnancy-related death among black and older women has not decreased from the late 1980s. The prevalence of complications and case-fatality rates

determine the pregnancy-related mortality. Investigation of biological, medical care, behavioral and system factors, which contribute to these disparities, is needed to develop strategies to reduce these gaps.

## Infant death among children whose mothers took folic acid during early pregnancy – Sino–US NTD Project

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Since 1991, women have been advised to increase their folic acid (FA) consumption to prevent neural tube defects (NTD); however, few studies have evaluated other health effects among children whose mothers took FA before and during early pregnancy. Subsequent to a program in China to prevent NTDs from which the authors knew whether or not women took 400 µg of FA before and during early pregnancy, the authors established prospective follow-up of these women and their children. The authors determined the number of deaths during the first year of life among singleton children born to these women. The authors identified 243779 eligible children, of whom 226494 (93%) were located; 2597 had died during infancy (11.5/1000 live births) and 3862 (1.6%) parents of the eligible children refused to participate. Among 120618 mothers who took FA and 105876 mothers who did not take FA, infant mortality rates (IMR) were 10.3 and 12.8, respectively (relative risk [RR], 0.80; 95% confidence intervals [CI], 0.74-0.86). For normal birth weight babies (2500-3999 g) for infants whose mothers did and did not take FA the RR was 0.78 (95% CI, 0.71, 0.86). Excluding infants who were born with major birth defects (N = 1338) the IMR for infants whose mothers did and did not take FA, were 8.6 and 11.0, respectively (RR, 0.78; 95% CI, 0.72, 0.85). In this population-based follow-up study, daily consumption of 400 µg of FA during the periconceptional period was associated with a lower risk for infant mortality in normal birth weight babies, which is not explained by prevention of birth defects by FA.

## Fertility and pregnancy among women who took folic acid during early pregnancy – Sino-US NTD Project

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Although consuming folic acid (FA) before and during early pregnancy reduces a woman's risk for having a baby with a neural tube defect (NTD), the effect of such FA use on fertility remains unclear. As part of a program in China to prevent NTDs (1993–95) we asked women to take a daily pill containing only 400 µg of FA before and during early pregnancy. From this project we knew whether or not each woman had used FA. In November 1998, we

used clinic records of women who had a premarital examination in 7 of 21 project counties to collect last menstrual dates (LMP) and outcomes of all pregnancies for each woman. For each woman whose LMP had occurred after their examination, we determined whether any LMP had occurred within 1 year of their examination and whether they ever delivered a child (up to 3.5 years followup). We calculated rates and risk ratios (RR) by pill use for eventual childbirth and for failing to have an LMP within one year of examination. Most women took FA (92%). Among pregnant women, 95% (21555/23351) had any pregnancy that ended with childbirth. Among women who had or had not taken FA, the rates did not differ (RR, 1.01; 95% confidence interval [CI], 0.99–1.01). Among all women who achieved pregnancy, 12% failed to do so within one year. Among women who had or had not taken FA these rates were 11.5 and 19.8%, respectively (RR, 0.58; 95% CI, 0.53-0.64). In this population-based, retrospective study of a cohort of healthy women beginning their reproductive lives, we found high rates of pregnancy and childbirth and no evidence that daily consumption of FA during early pregnancy influenced these women's risk for eventual childbirth. We do not know whether or not the reduced infertility the authors found among FA users was due to FA or to some other unknown difference between women who did or did not take FA.

#### Prevalence of autism in a United States population: Brick Township, NJ

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The authors determined the prevalence of autism spectrum disorders (ASD) in children 3-10 years of age residing in Brick Township, NJ at any time in 1998. The definition of autism spectrum disorders included autistic disorder, pervasive developmental disorder-not otherwise specified (PDD-NOS), and Asperger's disorder. The study used four sources for active case finding: special education records, records from local clinicians providing diagnosis or treatment for developmental or behavioral disabilities, lists of children from community parent groups, and families who volunteered for participation in the study in response to media attention. The autism diagnosis was verified or not verified for 71% of the children through clinical assessment. The assessment included medical and developmental history, physical and neurological evaluation, assessment of intellectual and behavioral functioning, and administration of the Autism Diagnostic Observation Schedule - Generic. The prevalence of all autism spectrum disorders combined was 6.7 cases per 1000 children. The prevalence for children meeting full diagnostic criteria for autistic disorder was 4.0 cases per 1000 children and the prevalence for PDD-NOS/Asperger's disorder was 2.7 cases per 1000 children. The characteristics of the children with autism in this study are similar to those described from previous studies. In the first recent US population-based study of autism, the prevalence of autism was found to be higher than previous US studies but the Brick Township prevalence is within the range of a few recent studies conducted outside the US that used intense case-finding methods.

#### Pregnancy outcomes in Canadian medical radiation technologists, 1950–2000

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A cohort of 12521 Canadian medical radiation technologists (MRTs) has been surveyed as part of a study to determine the relationship between adverse reproductive outcomes and level of occupational exposure to ionizing radiation. This cohort includes all individuals who were members of the Canadian Association of Medical Radiation Technologists for at least one year between 1994 and 1999, inclusive. The age at time of survey ranged from 23 to 82 years, with a median of 44 years. The majority of MRTs (87% of respondents) are female. Self-reported reproductive history was collected using mailed questionnaires. More than 11000 pregnancies were reported by female respondents, and almost 1800 by male respondents. Overall estimates of outcomes were similar to those expected, based on rates in the general population: e.g. low birth weight infants (<2500 g) comprised 5.0% of all births; 13.9% of all pregnancies ended with fetal death or stillbirth. However, these prevalence rates were observed to change over time, and to be different in men and women. For example, the percentage of pregnancies ending with fetal death or stillbirth increased in each decade, from 6.7% in the 1950s to 13.8% in the 1990s. Men consistently reported fewer fetal deaths and stillbirths (10.4% overall) than did women (13.8% overall). These differences may be due to gender differences in recall, and related to time-since-event; they may also point to some real changes over time. Detailed prevalence rates will be presented, and possible explanations for the observations will be explored.

#### The effect of birthweight discordance on individual twin mortality

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Birthweight discordance affects approximately a quarter of twin gestations, and is associated with perinatal death. As twin births continue to rise in the US, it is important to understand the contribution of this phenomenon to perinatal mortality. An NCHS matched multiple birth dataset file was used which contains all twin births in the US from 1995 to 1997. Birthweight discordance was grouped into four levels (15–19%, 20–24%, 25–29%, 30+%); mortality was defined as late fetal deaths plus infant deaths. Adjusted odds ratios (AORs) from logistic regression were used to estimate the risk of mortality from discordance, compared with the nondiscordant reference group, while controlling for gestation. This was done for all twins, and separately for the larger and smaller twin of each set. Mortality was 4 times higher among infants with a discordance of 30+% compared with infants with no discordance (139.0 and 31.1 per 1000, respectively). AORs ranged from 1.13 (95% CI = 1.05–1.21) among 15–19% discordant twins to 3.93 (95% CI = 3.77-4.23) among 30+% discordant pairs. Although this pattern was evident for the larger and smaller twin of each set, AORs were substantially greater among smaller twins (AORs ranging from 1.21 to 5.78) than among larger twins (AORs from 1.05 to 2.24). The smaller twin was also at greater mortality risk at every level of discordance. These trends were similar for white and black twins, although the influence of discordance was greater on white twins. While perinatal mortality risk among twins in general increases with increasing birthweight discordance, after controlling for gestation, the smallest infant of a twin pair is at disproportionate risk. Further examination of fetal growth is necessary to guide clinical practice.

# Rates of and factors associated with the recurrence of mental retardation, cerebral palsy, hearing impairment, and vision impairment – Metropolitan Atlanta Developmental Disabilities Surveillance Program, 1991–94

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The contribution of familial patterning to the overall prevalence rates and the factors associated with the recurrence of developmental disabilities is unclear. Data were utilized from the Metropolitan Atlanta Developmental Disabilities Surveillance Program to investigate the impact of the recurrence of developmental disabilities on the overall prevalence rates of mental retardation, cerebral palsy, hearing impairment, and vision impairment. Birth cohort prevalence rates in this study of mental retardation, cerebral palsy, hearing impairment and vision impairment in children aged 3-10 years are reported as 7.7, 2.1, 0.74, 0.69 per 1000, respectively. The contribution of recurrence to the overall prevalence is 5.8% for mental retardation, 2.0% for cerebral palsy, 3.5% for hearing impairment, and 3.7% for vision impairment. The rate of recurrence was significantly less for those cases whose sibling had multiple disabilities (5%) compared with those cases whose sibling had an isolated developmental disability (11%). Among the cases of isolated developmental disabilities with an affected sibling, 82% had the same developmental disability as their sibling. The contribution of recurrence to the overall prevalence for siblings with the same isolated disability as their sibling is 4.9% for mental retardation, 0.13% for cerebral palsy, 1.8% for hearing impairment, and 0.47%for vision impairment. Family size was significantly associated with recurrence for all developmental disabilities under study. Adjusting for family size, low maternal education, black race, and individual level and family level low birth weight were found to be associated with the recurrence of developmental disabilities. This information provides a better understanding of the population-based contribution of genetic and environmental factors in the etiology of developmental disabilities.

### The association between leisure-time physical activity and the delivery of a macrosomic infant

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Although the effect of maternal exercise on low birthweight has been the focus of investigation, there is a paucity of data regarding the association between exercise and macrosomic newborns. The authors investigated the effect of self-reported maternal physical activity on the outcome of macrosomia, defined as newborns weighing at least 4000 g, using a United States populationbased dataset. A case-control design was employed using data from the 1988 National Maternal and Infant Health Survey (NMIHS) that was restricted to non-anomalous, singleton infants who weighed 2500 g or more at birth. Cases (n = 524) and controls (n = 4639) were sampled on birthweight, and exposures to exercise and covariates were determined from sources available to the NMIHS. Associations were assessed with logistic regression adjusted for data-based confounders, with appropriate weighting for population inferences. Exercising women who were white, non-diabetic, or who gained less than 35 pounds were no more likely to deliver macrosomic infants than nonexercising women. A reduced risk of macrosomia was observed among black women (odds ratio [OR], 0.61; 95% confidence interval [CI], 0.43-0.87), women with glucose intolerance (OR, 0.25; 95% CI, 0.07-0.88), and obese women (OR, 0.55, 95% CI 0.29-1.01) who reported leisure-time exercise. A positive association between exercise other than walking and macrosomia was found for activity through the second trimester. These associations suggest that a reduced risk of macrosomia among exercising women depends on racial, metabolic, nutritional, and anthropometric factors.

#### The epidemiology of extrahepatic biliary atresia in New York State (1983–92)

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The etiology of biliary atresia, the leading cause of neonatal extrahepatic jaundice and the main indication for liver transplantation in children, is unknown. Research has focused on a viral etiology and development of murine infectious models. The few published epidemiologic studies report conflicting results for seasonal, geographic, and racial incidence variation. NYS Congenital Malformations Registry case data from 1983 through 1992 were matched to resident live births. County of residence, birth date, gestational age, birthweight, gender, maternal race, maternal age, and parity were identified. Chi-square statistics, relative risks, and 95% confidence intervals were calculated. Poisson regression and stratified analyses of New York City (NYC) vs. Other NYS were performed. The seasonality test of Walter and Elwood was used for month of conception and birth. 144 isolated or sequence event cases were ascertained, 0.52 (0.44, 0.60) per 10 000 live births. The relative risk in NYC was 3.66 (2.51, 5.34). The relative risk of fall vs. summer births was 1.83 (1.15, 2.92). The relative risk of spring vs. fall conceptions was 1.46 (0.91, 2.34). Seasonal patterns varied by region. In NYC, spring births and conceptions had highest risk, and month of conception was significant using the Walter-Elwood test. Fall/winter births and winter conceptions showed highest risk in Other NYS. The relative risk in black vs. white mothers was 2.16 (1.53, 3.05). Term low birthweight infants showed highest risk, 3.26 (1.83, 5.80). Higher incidence in a densely populated area and in cooler months supports an infectious hypothesis.

### Relationship between insulin resistance, weight gain and weight retention in pregnant women

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There is a growing concern that physiologic conditions during pregnancy may promote weight gain and postpartum (pp) weight retention in vulnerable women. As an example, stillgrowing adolescents evidence greater gestational gain and pp weight retention. Since insulin is known to stimulate lipogenesis, we examined the relationship of insulin resistance to gestational weight gain and pp weight retention in 573 non-diabetic pregnant women from Camden including growing (growers) and non-growing adolescents (non-growers) and mature gravidas (controls). After controlling for potential confounding variables there was a dose-response relationship between insulin resistance parameters and gestational weight gain, pp (4-6 weeks) weight retention and skinfolds in all subjects during trimesters 2 and 3 (P < 0.05). For example in trimester 2, insulin  $(\beta = 0.10 \pm 0.03 \,\text{kg/unit insulin})$  and the insulin/glucose ratio  $(I/G, \beta = 0.58 \pm 0.14 \text{ kg/I/G} \text{ unit})$  were significantly associated (P < 0.001) with pp weight retention. Growers had significantly higher insulin levels and I/G ratio and lower C-peptide/insulin molar ratio at trimester 2 compared with the controls and nongrowers (P < 0.05) and, as a consequence, gained and retained significantly more weight. Current data suggest that elevated insulin and I/G ratio were significantly associated with gestational weight gain and pp weight retention. Still-growing gravidas have increased insulin resistance that is exacerbated by reduced insulin clearance. Thus, the effects of insulin on lipogenesis and lipolysis may play an important role in gestational weight gain and pp weight retention.

#### Outcomes of neonatal intensive care unit survivors

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Advances in neonatal intensive care have led to increased survival. However, the rate of morbidity, especially among the smallest survivors, remains high. We examined the outcomes of all infants who were born alive between January 1997 and December 1998 and admitted to one of the six level III neonatal intensive care units (NICUs) serving the Kaiser Permanente

Medical Center northern California region. All infants admitted to the NICU for at least 24 h were identified and detailed information on patient demographics, antenatal history, neonatal illness severity, selected diagnoses and NICU procedures between birth and initial discharge home was abstracted from medical records. Among the population of 35751 inborn births, 4040 (11.3%) were admitted to the NICU. The proportion of very low birth weight (VLBW: <1500 g), low birth weight (LBW: 1500–2499 g), and normal birth weight (NBW: ≥2500 g) inborn infants requiring neonatal intensive care was 84%, 66%, and 7%, respectively. Of the 4501 inborn and outborn infants admitted to the NICU, 566 (13%) were VLBW, 1460 (32%) LBW, and 2475 (55%) NBW. Males (55%) outnumbered females, 13% were twins, and 44% were White, 16% Black, 18% Hispanic, and 19% Asian. Survival to discharge was 90% among VLBW, 95% among LBW, and 98% among NBW. Among the VLBW group, 59% had respiratory distress syndrome, 56% received surfactant, and 63% were on assisted ventilation. Chronic lung disease at 36 weeks postmenstrual age occurred in 16% of VLBW infants. Pneumothorax (7%), necrotizing enterocolitis (6%), and retinopathy of prematurity (1%) were relatively rare outcomes. While 80% of VLBWs had a CNS ultrasound, only 15% showed evidence of intracranial hemorrhage. Prevalence of these outcomes declined with increasing birth weight and gestational age.

#### State-specific unintended pregnancy rates

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In 1994, 49.2% of all pregnancies in the United States were unintended. While national data on unintended pregnancies are periodically reported, state estimates have not been calculated. By combining state vital records data for abortions and Pregnancy Risk Assessment Monitoring System (PRAMS) data for live births, we estimated state rates of unintended pregnancy in 1996 for Alabama, Georgia, Maine, South Carolina, Washington, and West Virginia. PRAMS routinely surveys representative samples of new mothers. We summed the reported number of abortions and number of women with a live birth in each state to estimate the total number of pregnancies. Intended pregnancies were defined as those live births for which the mother responded that the pregnancy was intended on the PRAMS questionnaire. Unintended pregnancies were defined as all abortions plus the live births for which the mother responded that the pregnancy was unintended. Unintended pregnancy rates were calculated by age, state, and race (where race was collected and numbers were adequate). The percent of unintended pregnancies in the six states varied from 46% to 61%. Unintended pregnancy rates ranged from 24.1 to 45.3 per 1000 women ages 15-44. Unintended pregnancy rates for white women in five states ranged from 22.1 to 30.5 and for black women in three states from 56.9 to 70.0. Women ages 20-24 years had the highest unintended pregnancy rates in all states (range 53.8-95.9). State-specific unintended pregnancy rates are useful in estimating need for family planning services, evaluating interventions, and monitoring trends over time.

#### Intendedness of pregnancy among active duty women in the US Army

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The objective of this cross-sectional study was to determine the prevalence of unintended pregnancy and the association of unintended pregnancy with social and demographic factors among a population of active duty women in the US Army. Participants consisted of 212 women who were on active duty at the time of conception and who gave birth to viable infants at a US Army hospital at Fort Hood, Texas. Prevalence of unintended pregnancy among participants in this group was 50.9% (95% CI 44.0-57.9) with 36.3% being mistimed (95% CI 29.8-33.2) and 14.6% being unwanted (95% CI 10.2-20.1). A further 14.2% of the women experienced ambivalence (95% CI 9.8-19.6). These rates were similar to the higher state rates seen by the CDC. Factors associated with unintended pregnancy among the military population differ from their civilian counterparts. In contrast to civilian studies, race/ethnicity was not associated with unintended pregnancy. Predictors of unintended pregnancy included military rank, with highest rates among younger, unmarried soldiers living in the barracks. The results of the research indicate that in the study population, race/ethnicity is not associated with unintended pregnancy and non-commissioned officers had a lower rate of unintended pregnancy than other rank groupings.

#### The racial gap in infant mortality widens as class inequality worsens: a United States phenomenon

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Dramatic increases in income inequality and associated adverse health outcomes have prompted active research in the past 10 years. Another area of inequality commanding public health attention in the United States is the gap between blacks and whites. Although race and income are closely linked in the political economy of the US, few reports have explored their interaction at the aggregate level. We studied trends over the past halfcentury using data from the US census and vital statistics. Results. Between 1950 and 1995, although the US infant mortality rate fell by 74%, the US position internationally deteriorated from 6th to 24th. The ratio of US IMR to the lowest national rate reported in each year (either Sweden or Japan, depending on the year) rose from 1.4 to 2.0. In parallel with this, the ratio of black to white IMR within the US rose from 1.7 to 2.4. On closer inspection, the B-W gap did not rise steadily: it increased from 1950 to 1960, leveled out and fell until 1975, then rose even more steeply to 1995. Income inequality in the US, as measured by Gini index, showed a similar pattern: it also fell until 1970, reversed by 1975 and then rose to an all-time high in 1995. Conclusion. Increasing income inequality in

the US is temporally associated with a worsening US international ranking in infant mortality. Both indicators track with widening racial disparities in IMR. These findings suggest that attainment of the year 2010 Federal Health Initiative goal to eliminate racial disparities in infant outcome will require deeper understanding of the relationship of race and class inequality.

#### Increased risk of developmental disabilities in children with major birth defects

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To quantify the strength of associations between each of four developmental disabilities (DDs) and specific types of major birth defects, the authors linked data from two independent surveillance systems, the Metropolitan Atlanta Congenital Defects Program and the Metropolitan Atlanta Developmental Disabilities Surveillance Program. Study subjects were children with major birth defects (N = 9142; born 1981–91 in metro Atlanta) and 3- to 10-year-old-children born 1981-91 in metro Atlanta and identified in 1991-94 with one or more of the following: mental retardation, cerebral palsy, hearing and vision impairment (N =3685). Among the 9142 children with a major birth defect, 657 (7.2%) had a serious DD compared with 0.9% in children born in Atlanta with no major birth defect (prevalence ratio [PR] = 8.3, 95% CI = 7.6–9.0). In general, the more severe the DD the higher was the PR. As anticipated, birth defects originating in the nervous system and chromosomal defects had the highest PR for a subsequent DD. For all other categories of birth defects, PRs were lowest when all major birth defects present were confined to a single category (i.e. isolated defects). PRs increased monotonically as the number of different birth defect categories represented by a child's defects increased. When children with birth defects were subdivided by birth weight, those with normal birth weight accounted for most of the increased risk. These data highlight the possible early prenatal origins of some DDs and suggest that the number of anatomical systems involved is strongly related to functional outcomes in children with birth defects.

#### The β-fibrinogen gene G-453-A polymorphism is a risk factor for Legg–Perthes disease

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Legg—Perthes disease is a pediatric hip disorder characterized by a flattening of the femoral head. Etiologic theories involve repeated vascular interruptions of the blood supply to the proximal femur resulting in venous occlusion with subsequent venous hypertension and bone death. To explore possible hemostatic mechanisms, the authors enrolled 55 cases of Legg—Perthes disease identified in a university orthopedic clinic and 56 healthy community controls matched to cases according to age, race, and

sex. Parents of subjects completed a questionnaire about their child's lifestyle and medical history. Blood was obtained and DNA extracted to determine the presence of genetic polymorphisms related to coagulation. Participants were predominantly white (93%), male (77%) and under age 16 (70%). The focus of the present analysis is to evaluate the relationship between Legg-Perthes disease and the β-fibrinogen gene G-453-A polymorphism that is positively related to fibrinogen levels. Assuming a dominant genetic model, individuals who possessed either the heterozygous or homozygous polymorphic genotype were 2.5 times more likely to have Legg-Perthes disease compared with those without the mutation (odds ratio [OR] 2.55, 95% confidence interval [CI] 1.2, 5.8). Additionally, cases were more likely to be exposed to passive smoke than were controls (OR 5.6, 95% CI 2.0,12.0). Separate analyses by smoke exposure revealed that the excess risk of the G-453-A polymorphism occurs in those exposed (OR 4.4) as opposed to those unexposed to passive smoke (OR 1.6). Although this difference in the ORs is not statistically significant, it suggests an interactive effect of passive exposure to cigarette smoke and the β-fibrinogen gene G-453-A polymorphism in the risk of developing Legg-Perthes disease.

#### Neonatal morbidity and mortality at 33–36 weeks' gestation

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To determine neonatal morbidity and mortality associated with preterm birth at 33-36 weeks' gestation, a retrospective population-based cohort study was conducted using the Nova Scotia Atlee Perinatal Database. Outcomes were examined among singleton births born between 1988 and 1999 in Nova Scotia, Canada. Infants with a major congenital anomaly were excluded. Neonatal morbidity and mortality among term infants (37-42 weeks' gestation) were compared with outcomes in preterm infants delivered at 33-34 weeks' gestation and 35-36 weeks' gestation. The neonatal outcomes analyzed were respiratory distress syndrome (RDS), hyperbilirubinemia, Grades 3 and 4 intraventricular hemorrhage (IVH), infection, asphyxia, and neonatal and infant death. Rate ratios (RR) were estimated from Poisson regression models and adjusted for confounding factors. The presence or absence of labor and type of preterm delivery (medically indicated vs. spontaneous) were evaluated as effect modifiers. The study cohort included 97497 singletons. Even among preterm infants delivered at 35-36 weeks' gestation, significantly increased risks were observed for all morbidity outcomes except IVH. The risk of RDS was markedly increased at 33-34 weeks (adjusted RR = 62.2; 95% confidence interval [CI] = 52.3, 74.1) and 35-36 weeks (adjusted RR = 17.3; 95% CI = 14.6, 20.6). Higher risks of RDS were observed for medically indicated preterm births at 35-36 weeks than for spontaneous preterm births at 35-36 weeks. The risk of neonatal and infant death was also increased among preterm births from 33 to 36 weeks' gestation, though only statistically significant for infant deaths. Knowledge of the increased neonatal morbidity associated with preterm birth at 33-36 weeks may assist prenatal care providers in clinical decision making and counseling.

#### Determinants of no prenatal care in HIV-infected women, selected US states, 1993–97

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Lack of prenatal care (PNC) is a key barrier to maximal reduction in perinatal HIV transmission. HIV surveillance data were matched to birth registries to identify 1839 HIV-infected women who delivered infants in CO, IN, LA, MI, MO, NJ, and SC between 1993 and 1997. Supplemental data were collected through review of maternal and infant medical records. Authors used logistic regression to identify determinants of no PNC in the overall population of HIV-infected women. Among a subset with ≥2 deliveries (n = 184), authors identified characteristics in the index pregnancy that were most predictive of no PNC in the subsequent pregnancy. Analyses were stratified by whether or not illicit drugs were used during pregnancy. In the overall population (n = 1839), 77% were black, 60% were age 20–29, 70% had parity ≥1 at index pregnancy, and 31% used drugs during the index pregnancy. Thirty-six percent of 563 HIV-infected women who used drugs during pregnancy and 7% of 1276 who did not use drugs received no PNC. For drug users, black race and parity ≥1 were predictors of no PNC. For non-drug users, parity ≥1 was predictive of no PNC. Among the subset of 184 women, the characteristic most strongly associated with no PNC in the subsequent pregnancy was no PNC in the index pregnancy. Among drug users, those with no PNC in the index pregnancy were 5.2 (P < 0.02) times more likely to receive no PNC in the subsequent pregnancy than women who received any PNC during the index pregnancy, controlling for age, race, parity, metropolitan status, and risk. Among nondrug users, the comparable effect measure was 9.5 (P < 0.01). Characterizing subgroups at risk for no PNC is critical for targeting outreach efforts and implementing programs to increase access to testing and treatment to eliminate perinatally acquired HIV.

#### Maternal smoking history and risk of hypertensive disease during pregnancy

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Background. Maternal smoking is associated with a reduced risk of hypertensive disease during pregnancy. Some studies suggest that a history of smoking before pregnancy also reduces a woman's risk. The authors examined the relationship between smoking before pregnancy and risk of developing hypertensive disease (gestational hypertension or preeclampsia). Methods. Data were obtained from the trial of Calcium for Preeclampsia Prevention (CPEP), a randomized clinical trial conducted at five US medical centers from 1992 to 1995. Four-thousand-five-hundred-89 nulliparous normotensive women were monitored for development of gestational hypertension or preeclampsia from study enrollment (13–21 weeks) until delivery. Smoking history was collected at enrollment and was used to define four exposure groups: (1) never smoked; (2) quit smoking before last

menstrual period (LMP); (3) quit after LMP, but before study enrollment; and (4) smoking at time of study enrollment. **Results.** After adjustment for maternal age, race, body mass index, insurance status, and medical center, smoking at study enrollment was associated with a reduced risk of hypertensive disease (RR = 0.75, 95% confidence interval, 0.60–0.93). Women who quit smoking before pregnancy did not have a reduced risk (RR = 1.09, 95% confidence interval, 0.88–1.32). Results were similar when gestational hypertension and preeclampsia were examined separately. **Conclusions.** Smoking before pregnancy does not appear to be associated with a reduced risk of gestational hypertension or preeclampsia.

#### Neonatal screening for congenital dislocation of the hip (CDH)

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**Objectives.** 1. To determine the incidence of CDH false negative screens (CDH missed in the birth hospital) and relate this to the examiner's educational level, and 2. To compare treatment required by children whose CDH was missed at birth with that required by children whose CDH was detected in the birth hospital. Methods. A retrospective study of newborns born at the IWK Health Centre from 1990 to 1998 was carried out. Children diagnosed with CDH at birth and those presenting to the only pediatric orthopedics consulting service in Nova Scotia were identified using perinatal and orthopedic databases. Chart review of all infants with CDH was carried out to confirm the diagnosis of CDH at birth or at an older age after discharge from the birth hospital. Results. Congenital hip examinations at birth were performed on 53 348 newborns by clinical clerks, residents, family doctors and pediatricians. A total of 234 cases of CDH were diagnosed, an incidence of 4.4 per 1000 liveborns. CDH was not detected at birth in 41 (17.5%). The incidence of missed CDH was 0.77 compared with 0.03 per 1000 liveborns screened by a small group of highly skilled examiners in a previous report (Tredwell, Clin Orthop 1992; 281: 63). No significant difference between clinical clerks, residents, family doctors and pediatricians was found. 41.5% of infants with missed CDH required surgery compared with 4.1% of infants who's CDH was diagnosed at birth (P < 0.001). Conclusion. Children with CDH missed at birth compared with those diagnosed in the birth hospital were more likely to require surgery. These findings suggest that identifying CDH at birth has important implications in determining response to less invasive forms of therapy and highlights the need for skilled examiners to detect CDH at birth.

### Can cognitive deficits in children with congenital cytomegalovirus (CMV) infection be predicted?

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Children without symptoms of congenital CMV infection may have cognitive deficits due to congenital CMV infection.

However, not all children with asymptomatic congenital CMV (Asx-CMV) infection will have neurodevelopmental deficits and it is not known whether perinatal factors would identify those children with Asx-CMV infection who are more likely to have poorer cognitive function at school age. The purpose of this study was to determine if certain perinatal factors could identify children with Asx-CMV infection who are at increased risk of cognitive deficit following infection. Included in the study are 144 children with Asx-CMV infection who were born at University Hospital between 1988 and 1995. The children received either a Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI) if the children were 5-6 years of age or a Wechsler Intelligence Scale for Children (WISC-III) for children 7 years and older to evaluate their cognitive development. The study population was 92% African-American, 51% female, 97% low income and 80% were cared for in the well baby nursery with a hospital stay of ≤3 days. The mean full scale IQ score (FSIQ) for the group was  $84.0 \pm 12.7$  (range, 49–113). Also, the mean verbal and performance IQ scores were between 45 and 118. Factors such as length of nursery stay, fetal distress at delivery, jaundice, hypoglycemia or other conditions did not differ between infants with lower FSIQs (≤70) and those with normal FSIQs (>85). However, infants with lower FSIQs were more likely to be preterm (OR = 3.7, 95% CI, 1.0-14.2) and to have a lower mean birth weight  $(2719 \pm 674 \text{ g vs. } 3106 \pm 670 \text{ g}, p = 0.03)$  than infants with normal FSIQs. Children with an increased risk of cognitive deficits following Asx-CMV infection will likely not be identified by perinatal factors alone.

### The association of prenatal and maternal factors with HIV testing during pregnancy

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Since 1995, health care providers have been advised to provide counseling and voluntary testing to all pregnant women so antiretroviral therapy can be initiated to reduce the risk of motherto-child HIV-1 transmission, if indicated. To evaluate whether sociodemographic, behavioral, prenatal health care (PNC) factors predict testing, we analyzed data from 4 states (FL, NY, OK, WV) participating in the Pregnancy Risk Assessment Monitoring System (PRAMS) from 1996 through 1998. PRAMS is an ongoing, population-based mail survey that collects information from mothers who recently gave birth to a live-born infant by randomly sampling state birth certificates. Mothers were asked, 'At any time during your most recent pregnancy or delivery, did you have a blood test for HIV?' SUDAAN was used to compute state-specific prevalence estimates and adjusted odds ratios. Odds ratios were converted to risk ratios due to high testing prevalence. State response rates to the entire questionnaire exceeded 70% and sample sizes ranged from 3570 to 6174 across the 3-year period. From 1996 to 1998, the proportion of mothers reporting testing increased in all states (range: 58.6% [NY, 1996] to 83.9% [FL, 1998]) but the increases were not significant (P > 0.05). Adjusting for maternal demographics and health care factors, a PNC test discussion was most strongly associated with testing in state models [RR adj (95% CI): 1.60 (1.52, 1.66){FL}; 2.60 (2.29, 2.78){NY}; 2.73 (2.52, 2.86){OK}; 2.88 (2.68, 3.02){WV}]. Women who were not married and used a public PNC provider were more likely to be tested as well. State HIV prevention programs can use this information to encourage PNC providers to discuss testing with all of their patients and develop strategies to target populations that are missing an opportunity to be tested.

#### Growth of children whose mothers took folic acid during early pregnancy – Sino–US NTD Project

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Since 1991, women have been advised to increase their folic acid (FA) consumption to prevent neural tube defects (NTD) among their offspring. Few studies have examined whether children of women who consumed periconceptional FA had any long-term health effects. Subsequent to a program in China to prevent NTDs from which the authors knew whether or not women took a pill containing only 400 µg of FA before and during early pregnancy, the authors established prospective follow-up of these women and their children. The authors measured weight and height in a cohort of these children at 3 through 5 years of age. Mean Z-scores for height-for-age and weight-for-height were compared for children whose mothers did or did not take FA during early pregnancy. Among 243 779 live born, singleton infants born during the study period, 226 494 parents of children (93%) were located; 3364 (1.4%) had children who had died and 3862 (1.6%) had living children but refused to participate. Most children (96%) completed the examination. Weight-for-height was similar among children of pill takers and non-pill takers. Mean Z-scores for height-for-age for children of pill takers was -0.48 and for children of non-pill takers was -0.57 (P < 0.001), suggesting that children of pill takers may be slightly taller for their age than children of non-pill takers. In this population-based follow-up study, daily maternal consumption of FA before and during early pregnancy was associated with a small increase in height in children at 3 through 5 years of age. The public health significance of this association has not yet been determined.

## Occurrence of miscarriage among women who took folic acid during early pregnancy – Sino–US NTD Project

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Although taking supplements that contain  $400\,\mu g$  of folic acid (FA) before and during early pregnancy reduces a woman's risk of having a baby with a neural tube defect (NTD), the effects of FA supplements on other pregnancy outcomes remain unclear.

The authors examined whether use of FA supplements affects the occurrence of clinically recognized miscarriage (<20 weeks gestation). Subjects were women in seven counties of China who had participated in a FA campaign to prevent NTDs, who were planning to marry and who had a premarital examination before they became pregnant for the first time. The authors examined the risk for miscarriage among women who had confirmed pregnancies (positive urine pregnancy test) and who had or had not taken FA pills daily. The overall rate of clinically recognized miscarriage among women experiencing their first pregnancy was 8.7% (2045/23567). The rates of miscarriage among women who had or had not taken FA before and during the first trimester were 8.7 and 8.9%, respectively (risk ratio, 0.98; 95% confidence interval, 0.84-1.14). The distributions of gestational age at pregnancy diagnosis and at miscarriage were similar for both groups of women. In this population-based, retrospective study of a cohort of women whose use of FA pills before and during early pregnancy had been previously documented and who had been pregnant for the first time, the authors found no evidence that daily consumption of FA before and during early pregnancy influenced their risk for miscarriage.

#### Narrowing inequalities in infant mortality in Southern Brazil

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In Brazil, the association between high infant mortality rates and low social level has been determined by the high level of inequality in health, according to WHO. The objective of this study was to determine the trend in infant mortality from 1995 to 1999 according to the level of maternal education. It was a registerbased study of municipal databases set up in 1994. All livebirths (42381) and infant deaths (731) that occurred between 1995 and 1999 in Porto Alegre, Brazil, were considered. Five different social categories were defined according to quintile of incidence of low maternal educational level (<6 years of schooling) in all urban neighbourhoods. For each social category the trend of excess of infant mortality (number of deaths observed in each quintile less number of deaths expected divided by the total of livebirths in each quintile) was calculated using chi-square for trend and Poisson multivariate regression. The infant mortality rate decreased from 18.36 deaths per 1000 livebirths in 1995 to 12.20 in 1999 (chi-square for trend p < 0.001). There was a significant decrease in infant mortality rate in all social categories, but the less privileged category showed the most important reduction in incidence rate ratio (IRR) from 0.93 (0.73-1.70) in 1995/96-0.50 (0.39-0.65) in 1998/99. The excess of infant mortality in each social category from 1995 to 1999 tended to be zero due to an intense reduction in infant mortality in less privileged social categories. The findings showed a non-random decline in infant mortality, especially among mothers of low educational level. The intense decrease of infant mortality in less privileged social categories in Porto Alegre is in contrast to data for Brazil as a whole, a country with one of the highest levels of inequality in infant mortality in the world.

## Maternal social class, weight and length at birth and body mass index (BMI) in young adulthood MZ Goldani\*, LSB Haeffner, H Bettiol, MA Barbieri, AAM Silva

(University of Rio Grande do Sul, Brazil)

The authors conducted this study aiming to assess the influence of weight, length and maternal social class at birth on body mass index (BMI) in young adulthood. A cohort study was carried out in 1978 with 3468 mother-male child pairs in Ribeirão Preto, Brazil. Biological, economic and social variables were obtained after the delivery and anthropometric measurements were made on newborns. A total of 2048 males from the original cohort were contacted during the army recruitment at 18-years-old and height and weight were obtained in 1191 cases. The prevalence of overweight (BMI ≥ 25) and underweight (BMI < 20) was calculated according to maternal social class, weight and length at birth. Non-adjusted analysis was performed for each independent variable, and a linear regression model was performed using BMI as dependent variable adjusted for birth weight and length as continuous variables, and social class, maternal age and conscript schooling as categorical variables. BMI < 20 was found in 234 males (19.6%) and BMI  $\geq$  25 in 244 males (20.5%). The prevalence of underweight was inversely related to weight and length at birth. The prevalence of overweight decreased from 25.2% to 15.9% and mean BMI from 23.6 at a birth weight of >3999 g to 22.1 at a birth weight of <2500 g. There was a similar trend for length at birth. There was a decrease in the prevalence of overweight from 27.2% to 13.8% and mean BMI from 23.3 in high maternal social class to 22.2 in low maternal social class. In the multiple linear regression only birth weight was associated with BMI. The authors conclude that BMI was consistently influenced by birth weight. Overweight was associated with high maternal social class, high weight and length at birth, and underweight was associated with low maternal social class, low weight and length at birth.

#### Trends in low birth weight rate in Brazil

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Trends in low birth weight (LBW) rate in Brazil from 1994 to 1998 were studied using data derived from the SINASC (Live Births Information System). These are the first estimates available in the country as a whole, since Brazil did not have such a system before 1994. This system provides coverage of 87.2%, varying from 73.2% in the North-east to almost complete coverage in the South region. Validation studies showed that the reliability of birth weight recording is high. These estimates seem to be free from selection bias. Only infants with birth weights of 500 g or more were included. The LBW rate has dropped from 8.7% in 1994 to 7.9% in 1998, in contrast to what has been occurring in the US, where the rate has been recently increasing. For the whole period, LBW rates differed amongst regions, being lower in the poorest regions of the country (North and North-east) and higher in the richest ones (South-east and South), in sharp contrast to what was expected. Nevertheless, in 1997, infant mortality rates

(IMR) were lower in the most developed regions (24 per 1000 in the South) and higher in the less developed ones (58 per 1000 in the North-east). Higher underreporting of live births weighing less than 1500 g, reporting of live births with LBW as stillbirths in the poorest regions, and higher rates of maternal smoking and increasing use of assisted reproduction techniques in the richest regions may explain these discrepancies. Whatever the reasons, the current assertion that LBW reflects socioeconomic development may no longer be valid, at least for Brazil. The dissociation observed between LBW and IMR might be reflecting better perinatal care in the most developed regions of Brazil.

#### Sociodemographic risk factors among children with autism in metropolitan Atlanta, 1996

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Autism, a serious neurobehavioral disorder, affects up to 5/1000 US children. From 1991 to 1999, US children receiving educational services for autism increased 14-fold. Because reports are inconsistent about how sociodemographic factors affect the risk for autism, the authors conducted a case-control study of these risk factors and autism. Cases comprised 541 children with autism, born in 5 metropolitan Atlanta counties from 1986 through 1993, and identified at 3-10 years of age in 1996 by the Metropolitan Atlanta Developmental Disabilities Surveillance Program. Controls were Atlanta-born children without known developmental disabilities, randomly selected from vital records and frequency matched to case-children by year of birth. Sociodemographic variables were obtained from birth certificates and 1990 census. The authors conducted multivariate analyses by logistic regression (SAS). Preliminary results indicate that, case-children were more likely than control-children to be male (adjusted odds ratio [AOR] = 3.3, 95% confidence interval [CI] = 2.5-4.4), a multiple birth (AOR = 4.0, 95% CI = 1.7-9.1), or African-American (AOR = 1.7, 9.1)95% CI = 1.2–2.4), and their mothers were more likely to be >35years (AOR = 1.7, 95% CI = 1.1-2.7), have one previous live-birth (AOR = 1.5, 95% CI = 1.1-2.0), or have higher income (AOR = 2.3, 95% CI = 1.1-2.0)95% CI = 1.5–3.5). However, specific sociodemographic factors differed among children with isolated autism (autism with no other developmental disabilities) and non-isolated autism (autism with other developmental disabilities). Autism is significantly associated with certain sociodemographic risk factors. Further work is required to determine how sociodemographic factors affect the risk for autism, including how these specific factors differentially affect the risk for non-isolated vs. isolated autism.

## Unintended pregnancy in a commercially insured population

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**Background.** Unintended pregnancy in the US is a widespread problem with serious consequences for individuals, families and

society. While much research has focused on unintended pregnancy among minority and low-income populations, little is known about its prevalence in other populations. This analysis describes the prevalence of unintended pregnancy and associated factors among commercially insured members in the California health plan of a national managed care organization. Methods. All women in the health plan ages 18-49 who delivered a live birth during a 6-month interval were eligible for the study. Telephone surveys were conducted after delivery to collect information on demographic factors, pregnancy history, intendedness and use of birth control. The authors report the rate of unintended pregnancy and describe its association with demographic and pregnancyrelated factors. Results. Of the 1173 pregnancies, 29% were unintended. While the highest risks for unintendedness were observed in usual risk groups (age 18–24 years; Hispanic, African American or other race; single marital status; education <12 years; income <\$40 000; and interbirth interval <24 months), almost half of the unintended pregnancies were among married women with ≥12 years of education and >\$40000 income. Only 40% of the women with an unintended pregnancy reported using birth control in the month before conception, and almost two-thirds used less effective methods such as condoms and diaphragms. Conclusions. Even in a population where the majority of the women were married, highly educated and with incomes over \$40 000, almost one-third of the pregnancies were unintended. Since the majority of these women used no birth control or a less effective method, there may be opportunities for education and counseling.

#### Does infection during infancy protect against atopy?

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Background. Ecologic and small individual-level observational studies suggest that early exposure to infection 'programs' Thelper (Th) cells into the Th-1 pathway, thereby reducing the risk of subsequent atopic disease. Methods. Two case-control studies nested within a large (n = 17046) randomized trial of a breastfeeding promotion intervention in Belarus. Healthy, full-term, breastfed infants were enrolled at birth and followed up at 1, 2, 3, 6, 9, and 12 months (96.7% follow-up at 12 months), with detailed data collected at each visit on gastrointestinal (GI) and respiratory infection and on atopic eczema and wheezing, using standard clinical algorithms. The two case groups were defined as (1) first occurrence of atopic eczema and (2) second episode of wheezing, with incidence density sampling to select 4 controls born at the same maternity hospital for each case. To ensure temporal precedence of exposure, the latter was defined as one or more episodes of GI or respiratory infection (examined separately) with onset >7 days prior to onset of the case's atopic outcome. Results. For atopic eczema, there were 819 cases and 3276 controls. Prior exposure to respiratory infection occurred in 11.1% of cases vs. 27.7% of controls [OR = 0.33 (95% CI = 0.26-0.41)], whereas the corresponding figures for GI infection were 1.8 vs. 3.8% [OR = 0.47 (0.28–0.81)]. For recurrent wheeze (n = 185 cases and 740 controls), prior respiratory infection occurred in 24.9 vs. 37.0% of cases vs. controls [OR = 0.56 (0.39–0.81); for prior GI infection, exposure occurred in 1.6 vs. 3.1% [OR = 0.51 (0.15–1.73)]. **Conclusions.** These two large case-control studies offer strong support for the hypothesized 'clean environment' immunopathogenesis of atopic eczema and recurrent wheeze, even in a country with a very low incidence of atopic disease.

## Risk factors for spontaneous preterm birth among aboriginal and non-aboriginal women in Manitoba MI Heaman\*

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In Manitoba, the incidence of preterm birth (PTB) has been increasing and is about 25% higher among aboriginal (AB) women compared with non-aboriginal women. The purpose of this study was to identify risk factors for spontaneous PTB in Manitoba women, and to compare risk factors among AB and non-AB women. A case-control study was conducted at two tertiary care hospitals. Cases delivered a live singleton infant <37 completed weeks gestation, and controls delivered between 37 and 41 completed weeks gestation. A ratio of two controls per every case was used, and stratified sampling by race was employed. A survey interview was conducted with each subject on the postpartum unit, and information was collected from the health record. Data were analyzed using SPSS and SAS. There were 226 cases (36% AB) and 455 controls (38% AB). Using stratified analysis, significant risk factors for PTB across strata were previous PTB (odds ratio 4.4), antenatal hospitalization (3.9), vaginal bleeding (2.6), gestational hypertension (2.5), >2 spontaneous abortions (2.1), weight gain <20 pounds (2.3), inadequate prenatal care (2.1), and smoking prior to pregnancy (1.5). Significant risk factors for the non-AB stratum were abuse during pregnancy (4.6), low social support (4.2), low self-esteem (3.3), rupture of membranes (ROM) before labor (2.0), and moving >2 times in last year (1.9). Risk factors for the AB stratum were ROM before labor (6.3) and perceived stress (2.5), while age <19 years was protective (0.4). Multiple logistic regression models will be presented. This study contributes to our understanding of differences in risk factors among AB and non-AB women. Most biomedical risk factors demonstrated homogeneity of effect, while psychosocial risk factors demonstrated heterogeneity of effect across AB and non-AB strata.

#### Regional variations in preterm birth rates: the contribution of sociodemographic factors

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Although extensive research has identified individual risk factors for preterm birth (PTB), there has been less emphasis on ecologic studies of factors related to PTB. The purpose of this

study was to analyze regional variations in PTB rates in Manitoba and assess the contribution of sociodemographic factors on distribution of PTB. Using a geographic information system (GIS), Manitoba was divided into 61 different regions, called 'Population Health Research Areas' (PHRA). Data were obtained from the Manitoba Health perinatal database (1989-98) and the 1996 Canadian Census. Multiple regression techniques were used to study the relationship between selected ecologic variables and the incidence of PTB for each PHRA. The provincial PTB rate for 1989-98 was 6.6%. Differences in age-adjusted PTB rates occurred across the PHRAs (range 3.78% to 9.46%). The PTB rate was significantly higher in the urban area (6.86%) than the rural area (6.02%). Of the sociodemographic variables, family income (Pearson r = 0.28), ethnic composition (r = 0.46), immigrant status (r = 0.30), and unemployment (r = 0.57) were significantly associated with the PTB rate, while education was not. The PTB rate also was related to smoking during pregnancy (r = 0.51). Geographic regions with the highest rates of PTB were those with the highest prevalence of low average family income,% of population aged 15-64 years unemployed,% reporting Aboriginal ethnic status, % immigrants, and percentage women who smoked during pregnancy. Using multiple regression, the variables percentage unemployed, urban living, and smoking accounted for 51% of the variance in PTB rate. Thus significant regional variations in PTB were partially explained by sociodemographic factors. These factors require consideration when developing policies and programs aimed at reducing PTB

#### Short hospital discharge and breastfeeding duration: California, 1999

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Background. Despite recommendations that mothers breastfeed for at least one year, most women who begin breastfeeding stop after only a few months. Many women encounter problems early in the neonatal period that may lead to discontinuation of breastfeeding. The trend toward shorter stays in the hospital may be associated with difficulty resolving early breastfeeding problems. Methods. Data were drawn from the 1999 California Maternal and Infant Health Assessment, a statewide stratified random sample survey of 3483 childbearing mothers, weighted to represent all childbearing women in the state. Survival analysis was used to examine the relationship between one-day hospital stay at delivery and length of time breastfeeding, controlling for confounders. Mothers reported their infant's age when they stopped breastfeeding, which was used to calculate length of time breastfeeding; those still breastfeeding at the time of the survey were censored. Results. Twenty-nine percent of mothers in the sample had a one-day hospital stay. Mothers reporting a one-day stay, compared with mothers with other lengths of stay, had a significantly shorter reported time breastfeeding (adjusted RR, 0.85, 95% confidence interval 0.74, 0.99). Additional bivariate predictors of shorter time breastfeeding

included receipt of Medi-Cal for prenatal care; African-American, Asian/Pacific Islander, or Hispanic ethnicity; low education level; low income; second or later birth; maternal foreign-born status; and smoking during pregnancy. **Conclusions.** Despite the new laws requiring reimbursement for a 48-h postpartum stay, many women continue to leave the hospital early. Short stays may not provide adequate time to overcome problems women encounter when breastfeeding.

### Discordancy and catch-up growth in twins through age 3 years

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In an ongoing follow-up study of twins, 73 pairs (146 children) born between 1996 and 98 were measured for length (LT) or height (HT), weight (WT), and head circumference (HC). The purpose was to evaluate whether intrapair differences at birth persist through 3 years. Of the twins followed to date, 38 pairs were measured at 8 months, 40 at 18 months, and 15 at 3 years. The intrapair difference in WT at birth averaged 275 g, with the larger twin averaging 2529  $\pm$  581 g (birthweight z-score -0.22  $\pm$ 0.70 SDU) and the smaller 2244  $\pm$  583 g (-0.86  $\pm$  0.67 SDU). At 8 months there were significant differences in WT z-scores (+ 0.50  $\pm$  0.73 SDU, p < 0.01) and HC (+0.43  $\pm$  1.07 SDU, p < 0.05) favoring the larger twin, and a borderline difference in LT ( $\pm 0.30 \pm 1.06$ SDU). The lighter twin was still lighter ( $-0.30 \pm 1.17$  SDU vs. +0.08± 1.30 SDU), but demonstrated more rapid catch-up growth compared with the heavier twin (+0.63  $\pm$  1.20 SDU vs. +0.35  $\pm$  1.29 SDU from birth to 8 months, p < 0.01). By 18 months, the differences in HT ( $\pm 0.80$  SDU) and HC ( $\pm 0.28 \pm 1.28$  SDU) favoring the larger twin were much less, and only the difference in WT was still significant ( $\pm 0.38 \pm 0.87$  SDU, p < 0.05). Likewise, at 3 years, the twin born heavier was still heavier ( $\pm 0.43 \pm 0.56$  SDU, p < 0.01), but there were no significant differences in HT (+0.17  $\pm$  0.83 SDU), and almost complete catch-up in WT relative to the CDC/NCHS reference even for the lighter twin, with the twin heavier at birth averaging  $+0.51 \pm 0.81$  SDU for WT with catchup of nearly half an SDU ( $\pm 0.48 \pm 1.02$  SDU, p = 0.09), and the twin lighter at birth ( $\pm 0.08 \pm 0.97$  SDU at 3 years), catching up more than half an SDU ( $\pm 0.57 \pm 0.96$  SDU, p < 0.05). Thus, while relative intrapair differences, especially in WT, appear to persist through age 3, there is significant catch-up, with the twin smaller at birth catching up more than the larger.

#### Are short conception intervals associated with poor infant outcomes?

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In the US, demographic factors are associated with birth outcomes, although biological mechanisms are not clear. Using Minnesota's 1990–96 linked birth-death files, the authors examined

whether conception interval length might explain some demographic risk markers for infant low birthweight, preterm delivery, and survival. Multivariate analyses were conducted separately for 4866 adolescent and 210 108 adult multiparae. The mean conception interval length was 13 months for adolescents and 32 months for adults. Short interval length for adolescents was highest among those who were married and those with inadequate educations. Adolescent interval length was positively associated with birthweight (P = 0.009), but was not associated with other infant outcomes. For adults, short interval length was associated with younger age, married status and poor educational attainment. While adult interval length was positively associated with infant birthweight (P = 0.0001), low birthweight risk was highest among infants of women with either very short or long intervals. Interval length did not show clear patterns by maternal race for either age group. The stronger association of interval length with birth outcomes for adults could be because adolescent multiparae have little variation in interval length or because interval length has different influences for women of different ages. While it is often thought that interval length is not relevant to birth outcomes in well-nourished populations, the demographic patterns of short and long intervals in this study, as well as the association of intervals with some birth outcomes, suggest that interval length could signal factors other than nutrition in the US.

#### Fathers of infants born to adolescents: paternal characteristics and perinatal risks

WL Hellerstedt\*, PJ Johnson, M Stigler, JW Oswald, C Turnure

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This study describes (1) the characteristics of fathers of infants born to adolescents; (2) the associations of paternal characteristics with perinatal risks; and (3) whether the absence of paternal information on vital records is a maternal or infant risk marker. Data were from the birth certificates of 37155 singleton infants born to adolescents in Minnesota, 1990-96. Odds ratios and 95% confidence intervals were calculated from multivariate logistic regression analyses to describe the associations of paternal characteristics (educational adequacy for age, age difference from mother, race) with maternal prenatal behaviors (tobacco or alcohol use, prenatal care adequacy) and infant outcomes (low birthweight, preterm, small size for gestational age). Missing paternal data were coded as such and used in all analyses. Paternal data were missing for 41% of the infants; 21% of the fathers were younger than 20 years-old, 27% were adults no more than 5 years older than the mother, and 11% were adults more than 5 years older than the mother. About 20% of the fathers had inadequate educational attainment for age. Paternal characteristics were most strongly associated with maternal behaviors rather than infant outcomes. Paternal characteristics were not associated with low birthweight or preterm risk. Inadequate paternal education was associated with about twice the odds for small size for gestational age, maternal inadequate prenatal care and

prenatal smoking. Missing paternal age data, as well as teen paternal age, was associated with about twice the odds for inadequate maternal prenatal care and prenatal alcohol use. The absence of paternal data on vital records could identify high-risk families, and the current data encourage further exploration of the family environments of infants born to adolescents.

#### The reliability of maternal characteristics' data on birth certificates compared with self-report

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The reliability of data about prenatal substance use, prenatal care onset, maternal education and marital status was assessed by comparing data from a phone survey of 330 rural women at 6-14 months' postpartum with those from their infants' birth records. Percent agreement between the two sources was assessed with chi-square and kappa statistics; agreement was 97% for prenatal alcohol use, 88% for prenatal tobacco use, 81% for trimester prenatal care began, and 39% for month prenatal care began. Disagreement suggests that one source, and perhaps both, is not valid. 'Current' marital status was reported similarly for 86% of the sample and 'current' educational status was reported similarly for 89% of the sample, suggesting some real change in status or unreliability of reports. Multivariate logistic regression analyses, conducted separately for correlates of disagreement with each measure, generally showed that young maternal age, nonwhite maternal race, low educational attainment, and low household income were significantly (P < 0.05) associated with disagreement, as was maternal postpartum report that the pregnancy was mistimed or unwanted. Of interest was that the concentration of disagreement was among women at high demographic risk for poor birth outcomes. If the risk characteristics of such women are systematically misclassified, then etiologic research about the risk markers for poor birth outcomes could be biased. Because birth certificates are used to assess the magnitude of perinatal events, further work to estimate the degree and sources of misclassification on these records would enhance their utility in research, programming, and policy decisions.

## Risk of pregnancy-related hypertension and preeclampsia in relation to folic acid supplementation

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Hyperhomocysteinemia has been associated with hypertension in pregnancy and preeclampsia. Since folic acid supplementation can reduce homocysteine levels, the authors investigated the association between folic acid supplementation and pregnancyinduced hypertension and preeclampsia. The study population included US and Canadian women with non-malformed infants participating in the Slone Epidemiology Unit Birth Defects Study, 1993-2000. Women were interviewed within six months after delivery about sociodemographic and medical factors, and about multivitamin use in pregnancy and the occurrence of hypertension and preeclampsia. The authors compared exposure to folic acid-containing multivitamins among 136 women with hypertension (onset after 20 weeks of pregnancy) and 45 women with preeclampsia with exposure among 905 control women without a history of hypertension or preeclampsia who were ascertained the same year in the same geographic region. Relative risks (RR) were adjusted for weight, parity, and smoking, using conditional logistic regression. The multivariate adjusted RR of developing either pregnancy-induced hypertension or preeclampsia during the month following multivitamin supplementation, compared with not using multivitamins during that same month, was 0.59 (95% CI 0.38, 0.92). The RRs were 0.56 (95% CI 0.34, 0.94) for pregnancy-induced hypertension only and 0.71 (95% CI 0.28, 1.79) for preeclampsia. The effect of supplementation was stronger for pregnancy-induced hypertension that began before the 8th lunar month (RR = 0.18; 95% CI 0.04, 0.83) than for hypertension that began afterwards (RR = 0.64; 95% CI 0.36, 1.12). Folic acid supplementation during pregnancy may reduce the risk of pregnancy-induced hypertension.

### Levels of fetal fibronectin and interleukin-6 in vaginal fluid sampled in mid-trimester

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Introduction. Two biomarkers that may be indicative of an inflammatory process in pregnancy merit further investigation. Fetal fibronectin (FFN) is a protein produced in the fetal membranes and placenta. Levels of FFN in vaginal fluid have been positively associated with preterm delivery (PTD), primarily when sampled after 24 weeks' gestation. Interleukin-6 (IL-6) is a cytokine that is also detectable in vaginal fluid, but little is known about its relationships to FFN levels and to PTD. Methods. FFN and IL-6 levels were assessed in vaginal fluid sampled at 19-26 weeks' gestation from a subset of women (N = 196) enrolled in the community-based Pregnancy Outcomes and Community Health (POUCH) Study. Women were divided into two FFN groups, positive (>10 ng/mL) and negative (<10 ng/mL), and into IL-6 quintiles. The risk of PTD (delivery <37 week's gestation) was compared across the different groups. Results. The odds ratio (OR) for PTD in the 27 (14%) women who were FFN+ was 1.5 (95% CI 0.3, 5.3). IL-6 levels exhibited a 'U' shaped relationship to the risk of PTD. Using the 2nd and 3rd quintiles as the referent group, the PTD OR was 5.0 (95% CI 1.1, 30) for women in the 1st (lowest) quintile, 2.6 (95% CI 0.4, 18.2) for women in the 4th quintile, and 3.3 (95% CI 0.6, 22) for women in the 5th quintile. While women with high IL-6 levels were more likely to be FFN+, this combination did not confer excess risk of PTD. Conclusion. Vaginal FFN may be weakly associated with PTD when assessed at mid-trimester, but does not appear to be

a strong predictor. The 'U' shaped relationship between IL-6 levels and PTD may indicate that women who do not mount a sufficient inflammatory response and women with a highly active inflammatory response are both at increased risk of PTD.

#### Outdoor air pollution and childhood asthma in the United States

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Asthma can place a major burden on affected children and their families. Previous studies have focused on the association between outdoor air pollution and asthma prevalence and morbidity. The purpose of this study is to examine the association between chronic exposure to outdoor air pollutants and asthma prevalence and exacerbation in children residing in metropolitan counties in the United States. The authors linked asthma status information for children in the 1997 and 1998 National Health Interview Surveys with a county-level outdoor air pollution index, an aggregate index of measured levels of five pollutants. Of the 16 153 children included in the study, 938 (5.9%) had active asthma; further, 367 (36.9%) of the 938 children with asthma reported having at least one emergency room visit in the previous 12 months. The authors found that children living in counties in the upper three quartiles of the outdoor air pollution index were more likely to have active asthma than children living in counties in the lowest quartile (Adjusted OR 1.19, 95% CI = 0.93, 1.54). Similarly, among children with asthma, those living in counties in the upper three quartiles of the air pollution index had an increased odds of experiencing an asthma-related emergency room visit compared with children living in counties in the lowest quartile (Adjusted OR 1.69, 95% CI = 1.11, 2.59). This study suggests that residing in a metropolitan county with higher outdoor air pollution levels is associated with active asthma in children and with increased asthma-related emergency room visits.

#### An at-home collection protocol for measuring stress in pregnant women

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Introduction. The Pregnancy Outcomes and Community Health (POUCH) Study has developed an at-home data collection protocol designed to measure biochemical and physiological markers of stress. These measures will later be correlated with self-reported stress, environmental stressors, and pregnancy outcome. Here the authors report on the acceptability of this collection protocol and the merits of assessing biomarkers over multiple days. Methods. Pregnant women enrolled in mid-trimester from five communities were asked to collect urine and saliva

twice a day (waking and bedtime) for three consecutive days and to complete the Global Assessment of Recent Stress (GARS) scale daily. A subset of participants was given an opportunity to wear an ambulatory blood pressure monitor (ABPM) for 24 h. Salivary cortisol levels were analyzed in the first 245 women and compared across the three days. Results. Among the first 600 POUCH participants who were offered the at-home sample collection protocol, 504 (84%) consented. Of the 192 women who were offered the ABPM protocol, 138 (72%) accepted. The return rate for the sample collection kit was 95% (n = 481) and 100% for the ABPM. Women were assigned to quartiles based on their waking and bedtime cortisol value for each day. Across the three days, 35% of women had waking cortisol levels that did not stay within two adjacent quartiles and 25% of women had bedtime cortisol levels that did not stay within two adjacent quartiles. Conclusions. The at-home collection protocol was widely accepted. The results suggest that it may be important to measure cortisol values across more than one day among pregnant women.

### Prenatal glucocorticoid exposure and risk for cerebral palsy among low birth weight children

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Epidemiologic studies suggest that the risk for intraventricular hemorrhage and periventricular leukomalacia could be reduced in preterm/low birth weight infants by administration of prenatal glucocortocoids. The authors examined the association between prenatal glucocorticoid exposure and cerebral palsy in low birth weight children. The authors conducted a case-control study of 169 children with cerebral palsy and birth weight ≤1750 g, who were born in 1981–89, and identified at ages 3–10 years by the Metropolitan Atlanta Development Disabilities Surveillance Program. Control children (N = 231) were infant survivors without cerebral palsy, with similar selection criteria as case children. The type, dose, and timing of glucocorticoid use; selected maternal demographic, labor and delivery characteristics, and infant outcomes were obtained from hospital records. Multivariate analysis was performed using unconditional logistic regression. Twenty percent (78/400) of children were exposed to glucocorticoids: 12% of case children and 25% of control children. The authors found a strong protective association between prenatal glucocorticoid exposure and cerebral palsy risk, independent of major risk factors for cerebral palsy, in very low birth weight infants (adjusted OR = 0.42; 95% CI: 0.22, 0.79). A similar level of effect (but not statistically significant) was apparent for each type of glucocorticoid (dexamethasone or betamethasone) and by course of treatment (full or partial). The data suggest that prenatal glucocorticoid exposure is protective against long-term neurodevelopmental disabilities, specifically cerebral palsy, among low birth weight infants. Studies are needed to confirm and explore other possible neurodevelopmental outcomes and mechanisms of neuroprotective effect.

#### The burden of illness associated with triplet births

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Recent increases in multiple births and in their rate of preterm birth have led to concerns about the burden of illness associated with triplet and higher-order multiples. The authors examined rates of preterm birth and gestational age- and birth weightspecific fetal and infant mortality among triplet births in Canada. Information on triplet births was obtained from the linked stillbirth, live birth and mortality files of Statistics Canada for birth cohorts from 1985 to 1996. All triplet births in Canada (except those in Ontario and Newfoundland) were included. Two cohorts (1985–90 vs. 1991–96) were contrasted for assessing change using relative risks, 95% confidence intervals (CI) and P-values. 1459 triplet births were studied. Between 1985 and 90 and 1991-96, preterm birth among triplet live births increased by 6% (95% CI 3-9%) from 90.4% to 96.0%, respectively, those at 30-35 weeks' gestation increased from 55.9% to 73.4%, respectively, and live births over 35 weeks declined sharply. Fetal mortality was stable at 30.3 in 1985-90 and 33.8 per 1000 total births in 1991-96. Infant mortality among triplets declined from 112.7 in 1985-90-73.8 per 1000 live births in 1991-96 (35% decrease, 95% CI 9-53%). Infant deaths due to respiratory distress syndrome decreased from 35.9 in 1985-90-9.8 per 1000 live births in 1991–96 (P < 0.001). There were no deaths due to respiratory distress syndrome among triplet live births at 28 or more weeks' gestation in 1991–96. Infant deaths related to short gestation and low birth weight also decreased. In spite of reductions in infant mortality, a substantial burden of illness remains associated with triplet births because of very high rates of preterm birth and fetal and infant mortality. Fetal mortality among triplets has not decreased over the last decade.

## Changes in fetal and infant mortality due to increases in preterm birth among twins

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Recent increases in preterm birth due to increased obstetric intervention have been associated with declines in fetal deaths among singletons but not multiple births. The authors examined changes in preterm birth, and in gestational age- and birth weight-specific fetal and infant mortality among twins in Canada in order to explore this paradox. All twin births in Canada (except those in Newfoundland and Ontario) were included in the study, which was based on information from Statistics Canada's linked still-birth, live birth and mortality files. Changes in birth cohorts

between 1985 and 1996 were assessed using tests for linear trend, 95% confidence intervals (CI) and P-values. Logistic regression was used to control for changes in relevant determinants. 28 442 twin births were included in the study. The rate of preterm birth among twin live births increased by 17% (95% CI 14-20%) from 42.5% in 1985-87-49.6% in 1994-96. Overall fetal mortality rates declined but not consistently (p for trend = 0.09). Among twin fetuses at 34 weeks' gestation and over, however, fetal death rates decreased by 43% from 9.5 in 1985-87-5.4 per 1000 fetuses at risk in 1994–96 (P < 0.001). This was due to reductions in fetal deaths due to several causes including intrauterine hypoxia and birth asphyxia (60% decrease). Infant mortality declined significantly in all categories of gestational age above 23 weeks except 32-33 and 34-36 weeks. Infant mortality declines were due to reductions in deaths due to respiratory distress syndrome (53% decrease) and short gestation and unspecified low birth weight (69% decrease). Increased obstetric intervention at mild and moderate preterm gestation among twins has reduced fetal deaths through early delivery of compromised fetuses but may be slightly diluting reductions in infant mortality.

#### Non-specific effects of routine vaccines on child mortality: a case-control study

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Background. Vaccines may be associated with a non-specific activation of the immune system in areas with high mortality. Measles vaccines have shown to protect against measles, and also cause substantial reductions in child mortality from all causes other than measles by at least 30%. However, BCG (Bacille Calmette Guerine), DTP (diphtheria, tetanus, pertussis) and polio vaccines have shown opposite mortality trends. Evidence of their overall longterm effects on total mortality, particularly in areas of relatively lower child mortality with high vaccination coverage, is limited. This study examines such an association in a special project area of rural India. Methods. A population-based, case-control study was designed. Cases were children aged 12-59 months who died between 1st of January 1991 and 31st of December 1998. Controls (survivors) were chosen from a cohort of 15578 born in the same periods, matched individually by age, gender, family size and area of residence. Rigorous matching was possible using a computerised matching programme. Cases and controls (n = 325 pairs) were selected electronically from a complete and reliable database used for continuous surveillance of health parameters in the project area. Matched-pair and stratified analyses were done using EPI-INFO software. Results. There were no significant associations between BCG, DTP or polio vaccination status and child mortality [crude odds ratio (OR): 1.0; 95% confidence interval (CI): 0.5, 1.8; adjusted OR: 1.1; 95% CI: 0.7, 1.9], [crude OR: 1.6; 95% CI: 0.9, 2.8; adjusted OR: 1.7; 95% CI: 1.0, 2.7] and [crude OR: 1.2; 95% CI: 0.7, 2.2; adjusted OR: 1.4; 95% CI: 0.8, 2.3], respectively. Implications. This study demonstrates that routine childhood vaccines have important non-specific effects on child survival that should be considered when planning immunisation programmes in developing countries, and suggests the potential utility of 'total

mortality' as an epidemiological marker for future vaccine trials in high mortality areas.

#### The prevalence of developmental disabilities among multiple births in Metropolitan Atlanta

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Background. Twins and higher order multiples are at increased risk of intrauterine and neonatal death, as well as neurologic impairment compared with singletons. This study was conducted to examine the prevalence of cerebral palsy, mental retardation, and hearing and vision impairment, in multiple births. Methods. The study population included 3841 children with disabilities born in five counties of Metropolitan Atlanta between 1981 and 1991 and identified by the Metropolitan Atlanta Developmental Disabilities Surveillance Program at 3-10 years of age. A retrospective cohort of all infant survivors, born in the same years and geographic area, was used to determine birthweight- and plurality-specific prevalence rates for: all developmental disabilities combined, and individual disabilities, both overall and in the absence of coexisting disabilities. Results. Not accounting for birthweight, the crude prevalence of developmental disabilities overall (per 1000 infant survivors) was 10.1 in singletons (95% confidence interval [CI] 9.7-10.4) and 38.9 in twins (95% CI 34.6-43.4); a three- to seven-fold significant difference between twins and singletons was seen for each disability. Relative to singletons, the prevalence of cerebral palsy and mental retardation was twice as high among twins weighing 1000-1999 g and two- to four-fold higher among twins weighing 2500+g, while the prevalence of isolated cerebral palsy and mental retardation was significantly higher among twins only in the 2500+g birthweight group. Conclusions. Relative to singletons, there is an increased risk among normal birthweight twins for having cerebral palsy or mental retardation. Given recent increases in multiple births, these findings strongly indicate the need to identify risk factors for developmental disabilities in multiple births.

### Pregnancy outcome and disease progression in diabetic nephropathy: a surveillance program

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Diabetic nephropathy affects 40% of patients with insulin dependent diabetes mellitus. Progression to end stage renal disease occurs in 30% of those affected within 10–15 years. Although recent literature challenges the concept that pregnancy per se accelerates the natural course of diabetic nephropathy, the existing data are limited. The purpose of this surveillance program is to test the hypothesis that (1) the potential effect of pregnancy per se does not accelerate the natural course of renal disease in women with pregestational diabetes, and (2) pregnancy outcome is directly related to the severity of nephropathy as determined

by parameters of renal function. Pregnant women with diabetic nephropathy or related renal transplant are eligible for this surveillance program. A web site, www.med.uc.edu/diabetes, has been developed to facilitate enrollment and data collection. Nephropathy is defined as >500 mg protein/24 h before 16 weeks' gestation. Renal, medical and obstetrical history in addition to maternal and neonatal outcomes and complications are recorded. Laboratory test results are collected through pregnancy and at yearly follow-up. Pilot data were obtained from six centers for 16 subjects over a six-month period. Serum creatinine concentration range was 0.4-1.1 mg/dL and creatinine clearance 32-235 mL/min. Second and third trimester glycohemoglobin A1 concentration range was 5.2-7.3% (reference 4.7-6.4%) and gestational age at delivery 22-39 weeks. The potential effect of pregnancy on the natural course of diabetic nephropathy and its related morbidities is an important public health issue with many ethical concerns. To address this controversial issue, and achieve adequate statistical power, an international surveillance program with multiple recruitment sites is imperative.

#### Maternal pre- and postnatal influences on fetal growth and duration of pregnancy

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There is strong familial aggregation of low birthweight, with independent, additive contributions both from mother's birthweight and recurrence within siblings. Whether these are specific to fetal growth and/or mediated by length of gestation is unknown. The authors followed up 317 multiparous women (59 white, 258 black) born 1959-66 into the Philadelphia and Providence Collaborative Perinatal Project cohorts. 73 women were born preterm (<37 week), 71 small-for-gestational-age (SGA, <10th percentile) and 183 controls. Their 504 children were classified based on maternal SGA/preterm status and that of the index child (youngest of the sibling set). 9% of older sibs were SGA when neither was SGA, 16% if the mother only was SGA, 32% if the index child only was SGA, but 45% when both mother and index child were. Adjusting for race, maternal preterm status, smoking, and sibship size, the SGA risk in an older sib was 2.16 (95% CI 0.93-5.02) when the mother alone was SGA, 5.63 (95% CI1.61-19.70) if the index child only was SGA, and 10.27 (95% CI 3.56–29.64) with both SGA. In contrast, for preterm, with neither or mother only preterm, 10% and 11%, respectively, of older sibs were preterm, and the independent risk of preterm with mother only preterm was 1.04 (95% CI 0.46-2.36). However, when the index child or both mother and index child were preterm, 40% of older sibs were preterm. The adjusted risk of preterm in an older sib was 5.49 (95% CI 2.70-11.14) when the index child only or 7.12 (95% CI 2.64-19.22) when both were preterm. Both maternal birth characteristics (small size) and postnatal experiences (prior SGA children) affect fetal growth. Maternal birth characteristics (gestation at delivery) are less important, and postnatal experiences (prior preterm children) are far more important for preterm birth.

#### Risk of cancer in offspring of women who underwent *in vitro* fertilization

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In the past decade, attention has increasingly been focused on the long-term health effects of assisted reproductive techniques (ART), such as in vitro fertilization (IVF), on both the women and their offspring. Although the causes of childhood cancer are largely unknown, some studies suggest that prenatal factors (drug exposure) may play a role in the etiology of childhood malignancies. To determine the risk of cancer in children conceived by IVF we used a large population-based historical cohort initially designed to determine gynecological disorders in women who underwent IVF. The offspring of the initial cohort was included in the exposed cohort if they were conceived by IVF or other related fertility techniques (n = 9484). The unexposed group consisted of 7532 children whose mothers were diagnosed with subfertility disorders but were conceived naturally. A total of 16 childhood cancers were observed in the total study cohort whereas 15.5 were expected during a median follow up period of 5.1 years (Standardized Incidence Ratio [SIR] = 1.0; 95% confidence interval [CI] 0.6–1.7). In the group of children conceived after ART, the SIR was 1.1 (95% CI 0.5-2.2; 8 observed cases and 7.1 expected cases). Furthermore, a direct comparison between children conceived after ART and naturally conceived children revealed no increased risk for childhood malignancies (risk ratio [RR] = 0.6; 95% CI 0.2–1.6). Although the number of observed cancer cases are small, these findings demonstrate that children conceived by ART show no increased risk of cancer during childhood compared with the general population and our internal reference group.

#### Increased risk of hypospadias in male offspring of women exposed to diethylstilbestrol *in utero*

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Although transgenerational effects of diethylstilbestrol (DES) have recently been reported in experimental animals, no such studies have been done in human populations. The purpose of this study was to examine the risk of hypospadias in male offspring from women exposed to DES in utero. The study population consisted of all male offspring of a Dutch cohort of 16319 women diagnosed with subfertility problems. A mailed questionnaire to assess late effects of subfertility treatment was used to identify children with hypospadias. A total of 16319 mothers reported 8934 male offspring. There were 205 children whose mother reported DES-exposure in utero. Four of these children were reported to have hypospadias. Among all other 8729 children, only eight cases of hypospadias were reported, resulting in an increased prevalence ratio (PR) of hypospadias among the sons of DES-daughters (PR = 21.3, 95% Confidence Interval [CI]: 6.5-70.1). This increased risk for the sons of DES-daughters could not be explained by differences in maternal age or subfertility treatment. Children conceived after assisted reproductive technologies (ART), such as *in vitro* fertilization (IVF), were not at increased risk of hypospadias compared with naturally conceived children. Our findings suggest an increased risk of hypospadias in the male offspring of DES-daughters. Although the absolute risk of this congenital anomaly in DES-grandsons is small, the first observation of a transgenerational effect of DES in humans warrants additional studies.

#### Recurrence risks for non-syndromic cleft lip and/or cleft palate ( $CL \pm P$ ) using sibships in Missouri

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This study describes incidence, risk factors and recurrence risks for CL  $\pm$  P. Of 965 177 singleton live births, 1135 (660 boys, 475 girls) were identified with CL ± P through a maternally linked file of birth certificates and birth defect records in Missouri, 1980–97. The average annual incidence of  $CL \pm P$  in Missouri was 1.18 per 1000 births. Factors associated with increased risk of CL ± P in multivariate analysis included: small-for-gestationalage (SGA, odds ratio [OR] 1.35, 95% confidence interval [CI] 1.03-1.78), pregnancy complications such as hypertension and diabetes (OR 1.43, CI 1.12-1.83) and white vs. black race (OR 2.17, CI 1.49-3.12). Boys had higher risks than girls (OR 1.19, CI 0.98-1.45). Cigarette smoking and alcohol consumption during pregnancy were positively associated with  $CL \pm P$ , but did not reach significance (smoking OR 1.13, CI 0.90-1.41; alcohol OR 1.38, CI 0.51-3.72). Other non-significant factors were adequacy of prenatal care, maternal age, marital status, and interval between live births. Evidence for sibship aggregation of CL ± P was found using regressive logistic models after adjusting for sex, race/ethnicity, SGA status and pregnancy complications. The OR was 15.3 for sibship dependency on the eldest child (OR 12.5 if eldest was male compared with 19.1 if female). The OR was 18.8 for sibship dependency on the immediately prior child, with OR 26.8 for male/male or female/female siblings vs. 11.4 for male/female or female/male siblings. The risk of  $CL \pm P$  to a subsequent sibling increased 11.5 times for each affected older sibling. Consistent with some earlier reports, the risk of CL  $\pm$  P was reduced by change of residency or father: the percentage of affected younger siblings decreased from 6.8% to 1.7% if residency changed, and from 6.0% to 0% if the father changed.

#### Breastfeeding and growth: biology or bias?

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**Background**. Observational studies reporting lower infant weight and length by 6–12 months of age in infants with prolonged, exclusive breastfeeding cannot separate the effects of

feeding from selection bias and confounding by maternal attitudinal factors. **Methods.** Cluster-randomized trial (n = 31 clusters, 17046 healthy, term mother-infant pairs) of a breastfeeding promotion intervention, with follow-up at 1, 2, 3, 6, 9, and 12 months of age (96.7% at 12 month). Data were analyzed after stratification by region and urban vs. rural status and a multivariate mixed model to account for repeated measures and withincluster correlation. Results. Infants from the experimental sites were significantly more likely to be breastfed from 1 to 12 months and far more likely to be exclusively breastfed at 3 months (43.3 vs. 6.4%; P < 0.0001). Despite nearly identical birth weights (3448) g, experimental; 3446 g, control), mean weight was significantly higher in the experimental group by 1 month; the difference increased through 3 months (6161 vs. 6059 g; P < 0.0001), declined slowly thereafter, and disappeared by 12 months. Z-scores increased in both groups vs. the WHO/CDC reference. Length followed a similar pattern (61.2 vs. 60.7 cm, P = 0.004 at 3 month). Observational analyses based on the same cohort showed very different results, however: a significant drop in z-scores after 3 months in infants with prolonged (≥12 month) and exclusive (≥3 month) breastfeeding and a significant rise in those weaned by 1 month. Conclusions. Reports of slower infant growth with prolonged, exclusive breastfeeding are likely to reflect selection bias and confounding. Our experimental data suggest that prolonged, exclusive breastfeeding may even lead to faster weight and length gain in the first few months, with no detectable deficit by 12 months of age.

## Communication difficulties among individuals with cerebral palsy in the NHIS Disability Supplement

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Cerebral palsy (CP), a chronic motor disorder first appearing early in life, is frequently accompanied by other neurological deficits. Disturbances of speech are thought to be the most common co-occurring condition. This study provides the first population-based estimate of communication difficulties among persons with CP in the US. For individuals 5 or more years old, levels of difficulty with expressive communication were: difficulty communicating so that non-family members understand (mild), difficulty communicating so that family members understand (moderate), and difficulty communicating basic needs to family members (severe). Difficulty with receptive communication was considered present for those who had serious difficulty understanding when others talk or ask questions. Communication difficulties were compared among persons with cognitive and/or sensory deficits in addition to CP (CP+), CPonly, or no CP. Individuals with CP + reported more communication problems (48%) than those with CP-only (17%) or those without CP (1%). Difficulty with expressive communication (26%) was more common than difficulty with receptive communication (15%). Severe speech disturbances were 90 times more common among individuals with CP than among those without CP (4.5% and 0.05%, respectively). Communication difficulties were elevated among individuals with CP, even among those

without mental retardation and hearing deficits that could impair communication via non-motor pathways. Whether the dysarthria in individuals with CP-only is due to emotional stress or to the musculature used for speaking could not be determined in this study. Nonetheless, this study highlights the great need for early intervention and assistive technologies, including communication boards and computer aids, for individuals with CP.

#### Use of hot tub or Jacuzzi during pregnancy and the risk of spontaneous abortion (SAB)

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To examine whether hyperthermia during pregnancy increases the risk of SAB, the authors analyzed the data from a populationbased prospective cohort study conducted in the population of Kaiser Permanente Medical Care Program of the Northern California region. During 1996-98, all pregnant women in the San Francisco area who had a positive pregnancy test and who decided to carry the pregnancy to term were eligible for the study. After 2729 eligible women were contacted, 1380 (50.6%) agreed to participate in the study and 1063 were finally interviewed. The median gestational age at entry into the study was 40 days. Use of hot tub/Jacuzzi during pregnancy was ascertained during an in-person interview conducted soon after a woman's pregnancy was confirmed. Pregnancy outcomes were ascertained for every participant. After adjustment for potential confounders using the Cox proportional hazard regression to account for variation in gestational age at entry, the exposure to hot tub/Jacuzzi during pregnancy was associated with 80% increased risk of SAB [adjusted rate ratio (aRR) = 1.8, 95% confidence interval (CI): 1.2-2.8]. The risk increased with increasing water temperature: [aRR = 1.5, 95% CI: 0.4–6.4 for temperature  $<100 \,\mathrm{F}^{\circ}$  and aRR = 2.6, 1.1–6.0 for temperature  $\ge 100 \,\mathrm{F}^{\circ}$ ]. The risk also tended to increase with increasing frequency of use and to be higher for those who used hot tub or Jacuzzi at an earlier gestational age. The effect of prenatal exposure to hot tub/Jacuzzi was stronger among susceptible women with a history of subfertility and/or multiple SABs. Our results suggest that prenatal use of hot tub or Jacuzzi at a temperature of ≥100 F° may increase the risk of SAB.

### Periconceptional multivitamin use and the risk of spontaneous abortion (SAB)

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To determine whether multivitamin use before and/or during pregnancy affects the risk of SAB, we examined data from a population-based prospective cohort study conducted in the population of Kaiser Permanente Medical Care Program Northern California region. During 1996–98, all pregnant women in the San Francisco area who had a positive pregnancy test at one of

the two facilities in the area and who decided to carry the pregnancy to term were eligible for the study. Among the 2729 eligible women contacted, 1063 (39%) were finally interviewed. The median gestational age at entry into the study was 40 days. Periconceptional multivitamin use was ascertained during an inperson interview conducted soon after a woman's pregnancy was confirmed. Pregnancy outcomes were ascertained for every participant. After adjustment for potential confounders using the Cox proportional hazard regression to account for variation in gestational age at entry, multivitamin use before and/or during pregnancy was associated with a more than 40% reduction in the risk of SAB [adjusted rate ratio (aRR) = 0.6, 95% confidence interval (CI): 0.4-0.8]. Multivitamin use reduced the risk of early SAB (<7 weeks of gestation) slightly more than the risk of later SAB  $(\geq 7 \text{ weeks of gestation})$ , aRR = 0.4 (95% CI: 0.2–0.9) and aRR = 0.6 (95% CI: 0.4–0.9), respectively. The effect of multivitamin use was greater among a high-risk population defined as women with a history of subfertility and/or multiple SABs. Our results indicate that periconceptional use of multivitamins may reduce the risk of SAB.

## Pregnancy complications among women who took folic acid during early pregnancy – Sino-US NTD Project

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Consuming 400 µg of folic acid (FA) before and during early pregnancy reduces a woman's risk of having a baby with a neural tube defect (NTD); however, the effects of such FA use on other pregnancy-related conditions are not well studied. A program in China to prevent NTDs asked women to take a daily pill containing only 400 µg of FA before and during early pregnancy. The authors analyzed pregnancy and FA pill-taking records of women who had enrolled at the time of their premarital examination, and compared the rates of pregnancy- and delivery-related complications among women who had or had not taken FA pills. Most of these women (80%) took FA pills and (95%) were delivering their first baby. In all women (N = 142 194), the reports of premature rupture of membranes (6.7%), placenta previa (0.1%), and fetal distress during delivery (12.8%) were generally low and not different from those who did or did not take FA. Among women who had or had not taken FA the rates of low birth weight (<2500 g) were 2.6 and 2.9%, respectively (risk ratio [RR], 0.91; 95% confidence interval [CI], 0.84-0.98). Among women who had or had not taken FA the rates of premature birth (<37 weeks' gestational age) were 5.6 and 6.5%, respectively (RR, 0.86; 95% CI, 0.82-0.91). In this population-based study of a cohort of women whose use of FA before and during early pregnancy was documented before the end of pregnancy, the authors found no evidence that such consumption of FA was associated with any complications of pregnancy or delivery and may be associated with small reductions in the occurrence of LBW and prematurity.

### Risk of maternal postpartum readmission associated with type of delivery and diagnosis

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The authors assessed the risk of maternal readmission associated with operative vaginal and cesarean delivery and diagnosis necessitating rehospitalization, compared with spontaneous vaginal delivery. A retrospective cohort study was conducted using the Canadian Institute for Health Information's Hospital Discharge Abstract Database for 1995-98, which includes data from all provinces excluding Nova Scotia, Québec and Manitoba. Subjects were women having singleton live births. Those admitted to hospital within 60 days following discharge for childbirth were identified through data linkage. A total of 30 878 women (3.2%) were rehospitalized. After adjusting for maternal age using logistic regression, women undergoing cesarean delivery were at a significantly increased risk for maternal readmission [relative risk (RR) 1.2; 95% confidence interval (CI) 1.2-1.3]. Obstetric diagnoses associated with increased risk of readmission following cesarean delivery included pelvic injury (RR 7.0; 95% CI 6.4-7.6), thromboembolic (RR 2.1; 95% CI 1.7-2.5), obstetrical surgical (RR 1.5; 95% CI 1.3-1.6) and major puerperal infections (RR 1.4; 95% CI 1.3-1.6). Increased risk of readmission following operative vaginal delivery was associated with pelvic injury (RR 1.7; 95% CI 1.6-1.8) and obstetrical surgery (RR 1.3; 95% CI 1.2-1.3). Women with cesarean delivery are at increased risk of maternal readmission related to several serious conditions. These women should receive a comprehensive assessment of health status before discharge and appropriate follow-up.

#### The impact of prenatal diagnosis and pregnancy termination on overall infant mortality in Canada

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Although prenatal diagnosis and selective termination of affected pregnancies has the potential for reducing infant deaths due to congenital anomalies, no previous study has demonstrated a population-wide impact on overall infant mortality. The authors used data on all live births, stillbirths and infant deaths in Canada (excluding Ontario) from Statistics Canada for the years 1991–97. Trends over the study period were estimated using relative risks, 95% confidence intervals (CI) and 2-sided *P*-values. The birth cohort-based infant mortality rate (including births <500 g) fluctuated between 6.4 and 6.2 per 1000 live births between 1991 and 1994, then dropped to 6.1 per 1000 in 1995 and 5.4 per 1000 live births in 1996. Infant mortality due to conditions such as SIDS and immaturity among live births ≥500 g declined between 1991 and 1995. The rate of infant death from congenital anomalies was stable between 1991 and 1995 but

declined by 20% (95% CI 8–31%) from 1.83 per 1000 live births in 1995 to 1.47 per 1000 live births in 1996. Fetal deaths due to pregnancy termination at <22 weeks increased substantially (255%, 95% CI 68–650%), as did fetal deaths due to congenital anomalies at <22 weeks gestation. A large decrease in infant deaths due to congenital anomalies was responsible for the most recent decline in infant mortality in Canada. Increasing use of prenatal diagnosis and selective termination of affected pregnancies is probably responsible for the decrease in congenital anomaly related infant mortality.

#### Serum ferritin associated with fetal growth in twin pregnancies

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Both low and high levels of serum ferritin have been implicated in poor fetal growth for singletons, but the diagnostic value of ferritin in twin pregnancies is not known. For this study, serial iron status measures and maternal weight gain were collected for 129 mothers of twins. The mothers were  $31.9 \pm 5.1$  y, mostly white (85%), primiparous (54%), and <2% smoked. Weight gain at 24 weeks (WG24) was  $12.4 \pm 5.1$  kg, twin birthweight  $2488 \pm 504$  g at  $35.5 \pm 2.3$  week. With the greater blood volume expansion in twin pregnancies, serum ferritin declined precipitously (P < 0.01). Adjusting for ethnicity and parity, ferritin was 63.1  $\pm$  $4.0\,\mu g/L$  in the 1st trimester (11 week),  $34.6\pm3.0\,\mu g/L$  in the 2nd (19 week),  $11.3 \pm 2.4 \,\mu\text{g/L}$  in the 3rd (29 week) and thus below the cutoff for defining iron deficiency (12 µg/L). WG24 was a significant predictor of twin birthweight (15.2 ± 5.2 g/kg weight gain, P < 0.005), and 3rd trimester ferritin levels were lower with increased WG24 ( $-0.18 \pm 0.07 \text{ kg/}\mu\text{g/L}$ , P = 0.01). Third trimester ferritin levels were  $16.1 \pm 1.5 \,\mu\text{g/L}$  and twin birthweight  $2344 \pm$ 72 g with WG24 < 9.1 kg. In contrast, ferritin was  $9.8 \pm 1.2 \mu g/L$ and twin birthweight 2581  $\pm$  55 g with WG24 >15.5 kg (P < 0.05). Levels of hemoglobin (g/dL) did not differ by WG24 level. In addition, fetal growth for twins was significantly diminished (P < 0.01) when ferritin levels were >14.2  $\mu$ g/L (2421  $\pm$  53 g), compared with  $<7 \,\mu\text{g}/\text{L}$  (2660  $\pm$  52 g). Thus, while mothers of twins may have 3rd trimester serum ferritin levels consistent with iron deficiency, these may be a clinical indicator of adequate fetal growth, as iron stores are utilized to support the growth of two fetuses. On the other hand, 'high' levels, which may still be well below ferritin values found in the 3rd trimester for singletons with good outcomes, may be an indicator of growth restriction for twins.

#### Prenatal nutrition and birth weight. A sib-pair study of pregnancy specific exposures

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The Dutch Hunger Winter (1944–45) is considered a classic 'natural experiment' of the effect of acute food restriction. Conceptions during the famine resulted in birth weights  $\sim\!100\,\mathrm{g}$ 

higher than expected, even accounting for differences in age and parity between women who conceived during the famine and women who conceived before or after the famine. This has been attributed to the effects of late-gestation or early postnatal food abundance after liberation. It might however, also reflect hitherto unrecognized effects of family specific attributes. If such factors are associated with development of adult disease, estimates of the long-term effects of prenatal undernutrition may be biased. We compared birth weights of women (probands) born 1944-46 with those of their elder (born 1921-44) or younger (born 1946-59) sisters (596 sib-pairs). The mean age difference between probands and sisters was 31 months. We adjusted for birth order and maternal age at delivery of both proband and sib and for a potential time-trend. Birth weights of women conceived during the famine did not differ from their sisters (mean difference 24 g; 95% CI: -135 g to 184 g), suggesting that maternal characteristics other than nutrition were the source of increased birth weights in this group of probands. Sib-pair studies may therefore offer an improved method of studying long-term effects of pregnancy-specific exposures because of the effective control for familial clustering of risk. The methodology is widely applicable to studies of the fetal origins hypothesis. In view of these findings, previously reported associations between birth weight and adult health may need to be re-examined.

#### Effects of occupational radiation exposure on timeto-pregnancy in Canadian medical workers

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Exposure to high levels of ionizing radiation has been shown to cause impaired fertility in atomic bomb survivors and patients receiving radiation therapy for various medical conditions. However fertility rates in individuals receiving low-level occupational exposures have not been determined. One objective of 'The Canadian Medical Radiation Technologist's reproductive health study' is to determine the relationship between prepregnancy occupational exposure and time to first pregnancy (TTP). The mean reported TTP for female MRTs is 7.9 months (median = 3 months; range = 0-240 months). The female MRTs were divided into two groups, those working, and those not working, prior to first pregnancy. A multivariable regression model was used to assess the effect of 'working' after controlling for maternal age. An increased maternal age is related to both a greater TTP, and to an increased likelihood of having worked. Overall, this model showed a decrease in TTP of 2.5 months associated with prepregnancy work exposure, and an increase of 7 months for each 10-year increase in maternal age. However, there was a highly significant interaction between exposure and maternal age: above age 30, prepregnancy work exposure was associated with substantially increased TTP, while in younger women work exposure had much less effect. The presentation will focus on an explanation of these preliminary findings, using more detailed radiation dose information.

#### Are abused women more or less likely to use health care services during pregnancy?

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Research estimates that 4-26% of women are physically abused during the year before pregnancy, and 4-8% are abused during pregnancy; however, little is known concerning how abuse affects women's use of pregnancy-related services. It may be that abuse prompts women to seek services for their injuries/problems; alternatively, violence-related sequelae (such as depression) may interfere with women's ability to access services. This research compares the use of several pregnancy-related services (prenatal care, childbirth classes, nutritional services, home health visits, hospitalizations during pregnancy, and parenting classes) between physically abused and non-abused women using data from the North Carolina Pregnancy Risk Assessment Monitoring System, a statewide representative survey of 2648 recently postpartum women. The prevalence of physical abuse was 6.1% during pregnancy and 6.9% during the year before pregnancy, with 8.9% being abused before/during pregnancy. Most of the abused women had been victimized by their husbands/partners (62%), followed by multiple persons (12%), family members (11%), other persons (9%), and friends (6%). Bivariate analyses found that abused women were less likely than non-abused women to receive particular types of services during pregnancy (timely prenatal care and childbirth classes), but were more likely to receive other types of services (home health visits, hospitalizations during pregnancy, and nutritional services). However, when logistic regression was used to model each type of health service use as a function of abuse status and the women's sociodemographic characteristics (including age, education, race/ethnicity, marital status, parity, and poverty), abused women did not differ significantly from non-abused women in their use of any of the types of services.

#### Ultrasound determination of gestational age alters pregnancy outcome measurements

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**Background.** The introduction of ultrasound dating of gestations has resulted in a secular increase in the rate of preterm birth in several large ongoing databases of births (Goldenberg, 1989, Kramer, 1998). To examine whether a systematic error is present between gestational dating by menstrual dates (LMP), and ultrasound derived dates (ULS), the authors examined data from a recent multicenter cohort of births, the Preterm Prediction Study. **Methods.** From 2929 singleton births in this study of risk factors for preterm birth, 1037 were excluded because of unsure LMP (n = 1033), or a non-plausible gestational age at birth (>48 weeks, n = 4). All participants had first or early mid-trimester ULS. Demographic factors associated with unsure LMP were: non-Black race, smoking, and education >12 years. Birth data derived from LMP and ULS were compared for: mean gestational age at birth,

preterm delivery at <35 and <37 weeks, and small-forgestational-age (SGA), by the criteria of Brenner. **Results**. Mean gestational age at birth was slightly less for ULS compared with LMP ( $P \le 0.0001$ ), with a median error gap of 3 days. Rates of preterm birth at <35 and <37 weeks were slightly but not significantly more for ULS. Rates of SGA (<tenth percentile) were less for ULS ( $P \le 0.0001$ ). The only demographic factor associated with the error gap in gestational age was education <12 years (P = 0.004). **Conclusion.** In this sample of low income parturients, ULS resulted in calculation of a slight but statistically significantly lower gestational age at delivery, did not significantly alter calculation of rates of preterm birth, and significantly decreased estimation of SGA birth.

#### Organophosphate pesticide metabolites in urine from preschool children with flu-like illnesses

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Pesticide exposure in young children is of great public health concern, particularly in agricultural communities. This pilot study evaluated the potential for unrecognized pesticide-related illness in a population assumed to be at risk for exposure to organophosphate (OP) pesticides. Children aged 2–4 years (n =108) with flu-like symptoms were evaluated in agricultural community pediatric clinics for the presence of OP metabolites. Six metabolites (alkyl and dialkyl phosphates) were measured in urine using tandem mass spectrometry. All metabolite levels were adjusted for creatinine. Only two children had levels below the limits of detection (LOD) and the range for the sum of the 6 metabolites was from <LOD to 768.7 p.p.b. (median = 28.5 p.p.b.). Higher levels were observed for metabolites of methyl OP compounds (median =  $20.0 \, p.p.b.$ ) compared with ethyl (median = 4.6 p.p.b.), suggesting possible agricultural pesticide exposure in these children. Nearly half of the children (45%) were diagnosed with upper respiratory infections at the index clinic visit. None of the 19 specific symptoms queried was significantly associated with total adjusted metabolite levels. No significant associations with total adjusted level were observed for gender, diaper use, age in months, or parent's report of recent pesticide exposure. While study children were found to be exposed to various OP compounds, exposure could not be directly related to symptoms.

This is an abstract of a proposed presentation and does not necessarily reflect EPA policy.

#### Effect of maternal age on the risk of infant mortality among twins

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Much attention has been paid recently to increasing rates of multiple gestation births and the increased risk of adverse perinatal

outcomes that accompany such births. The increase in multiple gestation birth rates has been concentrated among older mothers although increases have also been seen in all women over 20 years of age. While it has been well established that maternal age has a J- or U-shaped relationship with infant mortality among singletons, the effect of maternal age on the risk of infant mortality among multiple gestation births has not been reported. Using US vital statistics birth and death data from 1995 to 97, we sought to characterize the relationship between maternal age and infant mortality among twin births. As there were no differences by race, we report results for all races combined. In 1995-97, approximately 2.63% of births were twins with the lowest rate among the youngest mothers and the highest rate among the oldest mothers. The infant mortality rate overall was 5.9 per 1000 live births. As expected, maternal age had a U-shaped association with infant mortality among singletons. The highest rates were found for the youngest and oldest mothers. Among twins, however, there was a steep and negative relationship between maternal age and infant mortality with twins born to younger mothers experiencing the highest rate of infant mortality. Among mothers less than 20 years old, 5.27% of twin births resulted in an infant death as compared with 2.11% among births to mothers 30-34 years of age. The lowest rates were found among mothers 40-49 years old (1.67%). The possible immediate causes for this relationship will be examined: (1) differences in birth weight/gestational age-specific mortality, and (2) differences in the distribution of birth weight/gestational age.

#### Variation in human milk oligosaccharide profile and risk of diarrhea in breastfed infants

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Background. Laboratory data suggest that certain oligosaccharides found in human milk protect against specific causes of diarrhea, but studies in infants are lacking. Methods. The authors examined protection against stable toxin-producing E. coli (STEC) infection and diarrhea in a cohort of 93 breastfed Mexican infants from birth to the end of breastfeeding (median 9 months, range 0.7-24 months, 863 child-months of follow-up). Each week, fieldworkers collected infant feeding and illness data and stool samples, which were analyzed for pathogens. A maternal milk sample collected 1-5 weeks postpartum was analyzed for 2-linked fucosylated oligosaccharides (fucose linked by a1,2 glycosidic bonds) and for 3/4-linked fucosylated oligosaccharides (fucose linked only by a1,3 or a1,4 glycosidic bonds). Results. STEC infections were detected in 47 infants. The mean quantity of milk oligosaccharides was unrelated to infection status (STEC + stool) or presence of symptoms in STEC + infants, but the mean 2- to 3/4-linked fucosylated oligosaccharide ratio was lower (P < 0.01) in milk consumed by infants who were STEC + symptomatic (3.9  $\pm$  0.7[SE], n = 4) vs. STEC + asymptomatic (7.6  $\pm$  1.0, n = 43) or STEC- (7.5  $\pm$  1.0, n = 46). Further, infants whose milk had high (>6.0, n = 46) vs. low (<6.0, n = 47) ratios had fewer episodes of moderate-to-severe diarrhea from any cause (12.8 vs. 20.6 cases/100 child-months, Rate Ratio [RR] = 0.62, 95% CI 0.44, 0.88; P < 0.01); protection declined from RR = 0.5 in infants <3 months to RR = 0.8 after 12 months (P < 0.01). **Conclusion.** The a2- to a3/4-linked oligosaccharide ratio may be a marker for human milk molecules that protect against STEC and other causes of diarrhea. This study is the first to demonstrate that variation in human milk oligosaccharide profiles is significantly associated with risk of diarrhea in breastfed infants.

#### Comparison of risk factors for preterm delivery, preterm and term small-for-gestational-age births

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Purpose. To determine the association between 33 maternal and infant factors and the risk of preterm delivery (PTD), preterm and term small-for-gestational-age (SGA) births, we examined N = 76444 live births which occurred in Central and Northern Alberta between 1994 and 1997. Methods. Subjects and risk data were obtained from a computerized perinatal database. Logistic regression was used to estimate the independent effects of the study factors for PTD and fetal growth restriction. Adjusted odds ratios (ORs), 95% confidence intervals and etiologic fractions were estimated for the study factors. Results. PTD was associated with pre-existing chronic illness (diabetes, hypertension, renal disease), obstetrical history (nulliparity, previous SGA/PTDs, stillbirth or neonatal death, 3 or more abortions, and pregnancy complications (multiple gestation, anemia, hypertension, toxemia, bleeding, placenta previa, abruptio placenta). ORs were 1.6-19.4. Maternal age (35+ years), smoking and drug dependency also increased the risk of PTD. ORs were 1.3-2.5. Modifiable factors contributed 11% to the overall risk of PTD. SGA births were also associated with obstetrical and medical factors (ORs were 1.5-46.9). SGA births were associated strongly with several modifiable factors (low prepregnancy weight, poor weight gain, advanced maternal age, smoking, drinking and drug dependency. ORs were 1.3-3.1. Modifiable factors contributed 29% and 31% to the risk of P-SGA and T-SGA births. These results validate the heterogeneity of low birth weight: different models exist.

## Parental history and early onset type 2 diabetes among African-American and Latino children in Chicago

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Recent increases in childhood type 2 diabetes incidence rates have led to greater attention to the role of familial aggregation in diabetes etiology. The authors reviewed a population-based

dataset of insulin-treated diabetes among African-American and Latino children ascertained through hospital records in Chicago. Cases (N = 225) were diagnosed before 18 y and completed a comprehensive interview. A subset of 50 (22%) participants with features of early type 2 diabetes (Early 2) were identified using one or more of the following criteria: cessation of insulin therapy >2 y after diagnosis; use of oral agents; presence of obesity, acanthosis nigricans or polycystic ovarian syndrome; or denoted 'atypical' or 'type 2' on the medical record. Most patients, 74%, had no parental history of diabetes; 8% had only paternal; 14% had only maternal; and 3.5% had both maternal and paternal history. The mean age at diagnosis was progressively older among those who had no diabetic parent (8.96 y), only paternal (9.74 y), only maternal (11.32 y), or both (13.38 y, p trend <0.01). This pattern held for Early 2s, but not for type 1s. Early 2s were also significantly more likely to have a diabetic parent (only paternal, 15.1% vs. 5.8%, p < 0.03, only maternal, 26.4% vs. 8.9%, p < 0.01, or both, 9.4% vs. 1.6%, p < 0.04). This analysis suggests that a positive parental history of diabetes may be more strongly related to the etiology of childhood type 2 than to type 1 diabetes. Whether this is a reflection of genetic or behavioral factors is as yet unclear.

#### Risk factors associated with national underascertainment of unexpected infant deaths

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Studies based on state child fatality reviews assert that national estimates of deaths from child abuse and neglect have 30-50% underascertainment. Local review of unexpected deaths (trauma and SIDS) may cause delays in assignment of cause of death at the state level, resulting in cases submitted with unknown causes for national statistics. US linked and unlinked birth/infant death files for the years 1983-91 and 1995-96 were used to compare potential risk factors for 53 470 SIDS fatalities, 9071 unintentional injury deaths, 8097 deaths with unknown cause, and 3473 homicides. The RR of death from unknown causes tended to fall between risks for homicides and SIDS or unintentional injury, indicating contributions from all causes. In 1995-96, RRs for no prenatal care vs. care at 1-3 months were 6.8 for unknown cause, 9.2 for homicides, 4.6 for unintentional injury and 4.4 for SIDS; for married vs. unmarried, RRs were 3.0 for unknown cause, 4.2 for homicide, and 2.6 for unintentional injury and SIDS. Deaths from traumatic and unknown causes were more likely for the 1% of unattended births compared with attended (RR = 2.4 for unknown cause, 5.5 for homicides, 1.9 for unintentional injury, and 1.0 for SIDS). Among all deaths, only 2% were unlinked whereas 5% of homicides and 4% of deaths with unknown cause were unlinked. For deaths of unknown cause and for homicides, the death was more likely to occur in the first week of life if the death certificate could not be linked to a birth certificate (unknown cause: 44% of unlinked vs. 12% of linked; homicide: 62% of unlinked deaths vs. 7% of linked). We recommend coordination among child fatality review teams, local, state and national officials to reduce underascertainment and improve documentation on circumstances of deaths to aid our efforts for prevention.

#### Does birthweight difference predict success/failure of vaginal birth after cesarean section attempts?

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Objective. To determine whether the difference in birthweight (BW) can be used to predict the success/failure of vaginal birth after cesarean-section (VBAC) attempts in a population of women with one prior C/S for cephalo-pelvic disproportion (CPD). Methods. A multicenter retrospective cohort study was performed. Medical records of 8021 women who attempted VBAC at 17 community and tertiary hospitals were abstracted by trained nurses. We identified 1176 patients who had an initial C/S for CPD. We assessed whether the difference in BW between the initial CPD C/S and the VBAC attempt could be used to predict the outcome of a trial of labor (TOL). We calculated sensitivity, specificity, positive and negative predictive values (PPV and NPV) using several absolute and relative difference cutoffs. Results. The success rate of TOL was 61.2%. The mean difference in BW between the initial CPD C/S and VBAC attempt was -141.9 g (±19.6 g) in patients with a successful VBAC as compared with +23.6 g ( $\pm 24.3 g$ ) in patients with a failed VBAC (P <0.0001). Despite this difference, we could not identify a cutoff that yielded an acceptable trade-off between sensitivity and specificity. VBAC failure prediction when VBAC BW/CPD BW ratio >1.2 had a sensitivity of 11.6%, specificity 92.2%, PPV 48.6% and PPV 62.2%. Using a ratio >1.1 or an absolute difference of 250 g or 500 g did not yield better results. Conclusion. The difference in infant size between the initial CPD C/S and VBAC attempt cannot be used to counsel patients about the likelihood of success/failure of the VBAC attempt. Thus, ultrasound at term in women with a prior CPD C/S to determine eligibility for a TOL is not justified.

### Black-white differences in health care utilization among children with frequent ear infections

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**Objective.** To examine differences in patterns of and barriers to health care utilization between black and white children with frequent ear infections. **Methods.** Secondary data analysis was conducted using the 1998 National Health Interview Survey – Sample Child File. Data on 12 383 children under 18 years of age and 894 of them who were reported by the parent/guardian to have had 'three or more ear infections during the past 12 months' were analyzed. The data were weighted and analyzed to represent all children nationwide accounting for complex survey design. **Results.** Among children under 18 years of age, 7.6 and

6.2% of white and black children, respectively, had frequent ear infections in the past year indicating no significant difference (P = 0.08) in the prevalence by race. Among those with frequent ear infections, while more whites had no 'usual' place to go when sick (3.7%) than blacks (0.5%), there were significant differences in the type of place they go (e.g. 43% blacks and 18% whites go to clinic/health center). The affected black children also had higher rates of getting delayed care than the affected white children due to various reasons - most significantly because of transportation problems (13% vs. 2%) - and were more likely than whites to be not able to afford prescription drugs (10% vs. 4%). While no significant difference existed between the two groups in having seen a general medical doctor, 13% of the affected black children saw medical specialists and 4% had surgery, while 29% of the affected white children saw medical specialists and 14% had surgery in the past year. Conclusions. While almost all black children with frequent ear infections had a usual place of health care, they were significantly more likely to face barriers in obtaining the care, especially the more specialized care.

#### Income inequality and infant mortality in the United States

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Income inequality is associated with poor health outcomes in the US and elsewhere. This study examined whether the putative relationship between income inequality and infant mortality persisted across individual-level measures of maternal race and social position. A county-level measure of inequality, the Gini index, calculated using 1990 census data and divided into quintiles, was combined with 1989-91 linked infant birth and death data. Adjusted odds ratios (AOR) and 95% confidence intervals (CI) for the relationship between the index and two outcomes, infant mortality and normal birthweight (NBW) postneonatal mortality, were estimated within education and race groups, controlling for influences of maternal parity, age, and marital status. Among mothers with 12 years of education, infant mortality was higher among those in the upper quintile of inequality compared with those in the lowest (AOR = 1.42; CI = 1.36, 1.49). This relationship was weaker for mothers in other education groups: <12 years (AOR = 1.24; CI = 1.17-1.31); 13-15 years (AOR = 1.28; CI = 1.20-1.37); and, 16+ years (AOR = 1.28; CI = 1.18-1.38). Associations differed between black (AOR = 1.27; CI = 1.18-1.36) and white (AOR = 1.41; CI = 1.37-1.44) mothers; odds ratios were close to 1.0 among Asian, American-Indian, and Hispanic mothers. Patterns of association within education subgroups were similar among black and white mothers, while magnitudes were close to the race-specific estimates. There was no significant association between income inequality and NBW postneonatal mortality. These findings suggest that factors leading to income disparities within counties can affect birth outcomes for some mothers; however, given the lack of association for NBW postneonatal mortality, an outcome typically sensitive to social disparities, the mechanisms are unclear.

#### Disparities in exposure to air pollution during pregnancy

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The Institute of Medicine (IOM) recently reported that disadvantaged populations experience higher levels of pollution. This study asked whether infants at high risk of poor birth outcomes are more likely to be exposed to higher levels of air pollution. An EPA county-level air quality index, based on 5 pollutants, was merged with 1994-96 Natality files, successfully linking with 78% of the births. High- and low-risk births were defined using a composite measure derived from maternal age, education, parity, and marital status. Adjusted odds ratios (AOR) were used to estimate the risk of residing in the 10% most polluted counties as a function of maternal risk and race. Associations between air quality and birth outcomes (preterm birth and small-forgestational age [SGA]), were calculated, controlling for risk and race. Compared with low-risk mothers, high-risk mothers were over 50% more likely to live in the most polluted counties; the relationship decreased markedly when adjusted for maternal race (AOR = 1.07, CI = 1.06-1.07). Compared with white mothers, black and Hispanic mothers were over twice as likely to live in the most polluted counties; these relationships persisted after controlling for maternal risk (black AOR = 2.83, CI = 2.81-2.84; Hispanic AOR = 3.15, CI = 3.13–3.16). While the unadjusted odds of preterm birth and SGA were about 10% higher in the most polluted counties, the influence of air quality decreased when adjusted for risk and race (preterm birth AOR = 1.04, CI = 1.04-1.05; SGA AOR = 1.03, CI = 1.02-1.03). Consistent with the IOM conclusions, demographically high-risk infants are more likely to be born in counties with poor air quality than their counterparts, though this finding does not explain known disparities in preterm birth or SGA. Implications for subsequent child health need to be examined.

#### The importance of age at infant death distributions: an under-utilized perinatal indicator

J Petrini\*, K Damus, RB Russell, C Alter (National March of Dimes Birth Defects Foundation, White Plains, NY, USA)

In the 1990s, US infant mortality rates stratified by age at death revealed that about two-thirds of infant deaths occur in the neonatal period and the remainder in the postneonatal period. Deviations from this expected distribution require careful analysis, as interventions that decrease neonatal and postneonatal deaths are different. Further stratification of age at death by first hour, first day, first week and first month provide additional information, particularly if these distributions are compared with a reference distribution for the nation, and found to vary within a specific region for subgroups of the population such as by maternal age, race, ethnicity and plurality. Linked birth/infant death files from the National Center for Health Statistics, for the combined years 1996–98, were analyzed to provide reference age at infant death

distributions for three birthweight-categories (≥2500 g, 1500–2499 g, <1500 g). For all infant deaths it was found that 40% occur within the first day of life, with 14% occurring in the first hour. Among very low birthweight infants, more than 60% die within the first day following birth, compared with only 10% of not low birthweight infants. Infant death distributions by plurality, gestational age, maternal age and race/ethnicity and geographic region reveal important differences in infant survival around the time of birth. Comparisons of these national reference ages at infant death distributions with region-specific distributions implicate differences in access to care, health care systems for high-risk infants and medical management of infants.

#### Which infants are at risk for fatal neural tube defects in the United States?

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Despite efforts in the 1990s to prevent neural tube defects (NTDs) with periconceptional folic acid, including recommendations by the US Public Health Service that all women of childbearing age consume 400 µg of folic acid daily, compliance by the public and health care providers has not been impressive. Surveys conducted suggest improvement, but behavior change has fallen short of targeted objectives. However, as suggested in NHANES 1999 data, it is possible that blood folate levels are increasing (following 1998 mandated fortification of grain at 140 µg/100 g) which is encouraging, as the ultimate endpoint is to decrease the incidence and mortality from NTDs. Unfortunately, there is currently no national birth defects monitoring program in the US and approximately one-third of states have no program. The National Center for Health Statistics (NCHS) has published national trends in the occurrence of NTDs from birth certificates (1991-9). However, only about 14% of birth defects are captured using birth certificates. While also limited, the US death certificate provides data on causes of infant deaths, including NTDs and thereby provide a gauge for fatal NTDs. The results of analyses of infant deaths due to NTDs from NCHS linked birth/infant death files for the combined years 1995-7 will be presented and will highlight differences by maternal age, education, race/ethnicity, gestational age, birthweight, age at death and region. Findings suggest that Hispanic infants, Mexicans in particular, have the highest rate among racial/ethnic groups and multiples are 4 times as likely as singletons to die due to an NTD. Limitations of monitoring NTDs, including the exclusion of fetal deaths, opportunities for improvement and implications of these findings for evaluating campaigns will be discussed.

### Maternal smoking during pregnancy: not a stable phenomenon

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Many women smokers quit when they become pregnant. Some researchers have noted a tendency towards relapse in the 3rd trimester but quitting is generally regarded as an early and stable phenomenon. Many epidemiologic studies rely on average or one-time measurement of smoking. The authors examined smoking fluctuation during pregnancy in the Family Health and Development Project (FHDP), a prospective study of 92 pregnant women, and the National Health Interview Survey 1991 Pregnancy and Smoking Supplement (NHIS-S), is a population-based survey of women who had given birth in the previous five years. The authors examined categories of amount smoked for each month in the FHDP and fluctuations in overall smoking status (i.e. smoking vs. not) across pregnancy in the NHIS-S. Fluctuations in smoking status were substantial, only 11.5% of women in the FHDP had consistent smoking status throughout pregnancy. While many women quit or reduced their smoking upon learning of their pregnancy (58%), nearly half changed smoking status multiple times. In the NHIS-S, first quit attempts were most frequent in the 1st trimester (71%) but a substantial minority took place later, and 8% took place in the 3rd trimester. Nearly 40% of women made a serious quit attempt but 44% relapsed during pregnancy. Among women who quit for >1 week, the duration of time off cigarettes varied from 1 to 2 weeks (34%) to 8+ weeks (32%). Smoking during pregnancy is a complex and variable behavior for many women. Average or one-time measures of smoking may lead to substantial misclassification of fetal exposure. The determinants of smoking fluctuation and the significance of multiple variations in dosage and timing of exposure for predicting the risk of adverse outcomes deserve further

#### Birth characteristics of offspring and parental diabetes

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Several studies have shown inverse associations between birth weight (BW) and the risk of diabetes in adulthood. Diabetes and low BW may share common risk factors, e.g. genetic polymorphisms that generate associations between the two. A dataset was created by a record linkage between the Swedish Medical Birth Register and the Cause of Death Register. Birth data on all children born in Sweden 1973-80 were linked with their parents' death records. The dataset contained 573 437 mothers (93 diabetes deaths) and 563 008 fathers (302 diabetes deaths). Hazard ratios were estimated from proportional hazards regression models. Risks of parental deaths (RRs with 95% CI) were estimated per kg increase in BW. After adjustment for gestational age, BW of offspring was negatively related to diabetic mortality among mothers RR = 0.54 (0.35–0.83) and fathers RR = 0.78 (0.61–0.99). Early premature delivery was strongly related to diabetes mortality among mothers 3.66 (2.14-6.27) but not fathers RR = 0.73(0.40-1.33). Adjustment for educational level left the findings unchanged. Diabetic mothers tend to have higher BW babies than non-diabetic mothers, which should lead to an association in the opposite direction. A polymorphism associated with both low BW and diabetes might generate the observed association, although

the fetal environment of prediabetic or diabetic mothers including treatments could result in fetal growth retardation and premature delivery. The evidence for common polymorphisms for low BW and diabetes risk among fathers is stronger, since paternal diabetes will clearly not directly influence fetal growth.

#### Fetal growth is associated with parents' cardiovascular mortality

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Many studies have shown inverse associations between birth weight (BW) and cardiovascular disease (CVD) in adulthood. Intergenerational influences illustrated by correlations between the BW of parents and BW of their offspring, suggests that BW of offspring might be associated with CVD among parents. The authors studied this issue using the Swedish Medical Birth Register and the Cause of Death Register. Data for all children born in Sweden 1973–80 were linked with their parents' death records. The dataset contains 573 437 mothers and 563 008 fathers. We examined all-cause and CVD mortality up to 1997 using proportional hazards regression analysis. Risks of parental deaths (RRs with 95% CI) were estimated per kg increase in BW controlling for gestational age, parents' age, and level of education. Father's smoking habits at age 18 were also taken into account in a subsample (n = 21686). Maternal all-cause mortality was inversely related to offspring BW (RR = 0.72; 95% CI 0.69, 0.75). The association with paternal CVD mortality was weaker (RR = 0.84; 95% CI 0.82, 0.87). Maternal CVD mortality was strongly inversely related to offspring BW (RR = 0.58; 95% CI 0.51, 0.66) and the association with paternal CVD mortality was weaker (RR = 0.85; 95% CI 0.80, 0.90). Adjustment for level of education and paternal smoking left the findings virtually unchanged. The mother's growth, development and health from her own fetal life to adulthood may influence BW of offspring and CVD mortality. Genetic polymorphisms related to both fetal growth and CVD mortality or uncontrolled confounding due to life-style factors might also play a role.

## Residential proximity to dairies: effect on respiratory and gastrointestinal illness among children

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Occupational health hazards associated with exposure to agricultural contaminants have been documented but public health risks associated with dairy pollution is unknown. This study evaluated the association of residential proximity from a dairy farm with respiratory and gastrointestinal (GI) illness among children aged 1–17 years. Study participants were recruited from health-care clinics located in a low-income area dense with

dairy herds on the US-Mexico border. A semisupervised selfadministered questionnaire was distributed to the subject's parent/guardian to ascertain physical location of the home, child and maternal demographics, and household characteristics. Residential distance from a dairy was measured using GIS technology. Health outcomes were based on ICD-9 codes. Multivariate analysis showed no relationship between respiratory diagnosis and living near a dairy. After adjustment for relevant covariates, each one-kilometer increase in residential distance from a dairy was associated with a 20% risk reduction for GI diagnosis. The odds of respiratory illness significantly increased with report of rodents in the home and decreased with maternal education and child's age. Paved roads and no screens on windows each were significantly associated with GI illness while increasing child age showed a protective effect. These findings support recent studies showing that children exposed to a farm environment may be less prone to respiratory problems than children who live in nonfarming surroundings and suggest that xenobiotics discharged from dairy operations may pose a GI health threat to children living in nearby communities. Future studies that more precisely estimate exposure to dairy contaminants and health outcomes are needed to clarify the observed relationships.

#### Early childhood infections and the risk of acute lymphoblastic leukemia

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It has been hypothesized that children with an abnormal pattern of infectious disease acquisition, particularly delays in the timing of infections, are at an increased risk of acute lymphoblastic leukemia (ALL). Childhood infections before 25 months of age and ALL were assessed in a regional case-control study. Cases (n = 255) were <15 years of age when diagnosed at one of four referral centers between January 1980–December 1991. Controls (n = 760) were a random sample of births from the 31-county referral area, frequency matched by sex, race and birth year. Mailed questionnaires were completed by case and control parents. Infectious disease histories were censored at the age at diagnosis for cases and an equivalent age for controls. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated using unconditional logistic regression. Covariables included maternal education and smoking, ever breast-fed, allergy history (child), child care before two years and birth order. Cases and controls were predominantly white (95%) and male (56%); 50% were breastfed with 40% first-born. Illnesses reported before two years of age in cases and controls included: colds (85%), otitis media (57%), diarrhea (43%) and vomiting (29%); croup, influenza, bronchiolitis and pneumonia were reported in <15% of children. Diarrhea was associated with a reduced risk of ALL, with an OR (CI) of 0.75 (0.55-1.02). Early episodes of otitis media were suggestive of an increased risk, with an OR (CI) of 1.25 (0.93-1.69). The other respiratory illnesses and vomiting were not associated with ALL. These data provide little support for the hypothesis that delays in infection acquisition are associated with ALL.

#### Women with impaired glucose status during pregnancy have heavier babies

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The role of impaired glucose tolerance during pregnancy as a determinant of infant birth weight is controversial. This study examines the relationship of glucose intolerance during pregnancy to birth weight in participants of the Pregnancy, Infection, and Nutrition Study (PIN). This prospective cohort study recruited women from prenatal clinics in central North Carolina at 24-29 weeks gestation. Universal glucose screening at these clinics includes a 50-g O'Sullivan. Women who screened high (≥140 mg/dL) were given a 100-g oral glucose tolerance test (OGTT). Normal glucose tolerance (NGT) is defined as an O'Sullivan screen <140 mg/dL, impaired glucose tolerance (IGT) as one high value on the OGTT, and gestational diabetes (GDM) as 2 high values on the OGTT. Women with known glucose status and birth outcome information were included in this analysis (n = 1988). Mean birth weight was compared in the 3 groups using analysis of variance. Linear regression models were used to assess the relationship of IGT and GDM to birth weight, controlling for maternal prepregnancy BMI, age, race/ethnicity, and gestational age. IGT occurred in 2.3% of the sample, while 5.1% had GDM. Mean (SD) birth weights for the groups were: NGT: 3292 (617) g; IGT: 3608 (489) g; GDM: 3430 (609) g. Mean birth weight of infants whose mothers had IGT, was significantly greater than those of NGT mothers (316 g difference, p = 0.004). After controlling for mother's prepregnancy BMI, age, race, and gestational age, IGT remained a significant determinant of birth weight ( $\beta = 138 \,\mathrm{g}$ , p = 0.005) and GDM became significant ( $\beta = 98 \, \text{g}$ , p = 0.043). Results show that, independent of maternal prepregnancy BMI, impaired glucose tolerance enhances fetal growth rate. This raises the question of whether we should be treating IGT as well as GDM.

#### Comparison of pregnancy dating by last menstrual period, ultrasound, or their combination

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Date of conception estimates are subject to uncertainty. To compare results using pregnancy dating based on ultrasound (US), last menstrual period (LMP), or their combination (US + LMP), the authors analyzed data from women eligible for a cohort study of preterm birth, the Pregnancy, Infection, and Nutrition Study from two clinics in central North Carolina. 4978 women were identified, 478 with LMP information only, 557 with US only, and 3943 with both. Conception dates were estimated using LMP only, US only, and LMP overridden by US (LMP + US) when there was a 14- or 7-day disparity, invoked in 15% and 30% of women, respectively. The proportions <37 weeks' gestation were slightly greater for US and US + LMP (13.2%) compared with LMP alone (12.8%), whereas the proportion of births <34 or

<32 weeks was slightly higher with LMP estimates. The standard deviation of gestational age was greater for LMP (2.9 weeks vs. 2.4 for the others), and the correlation with birth weight was smaller (r = 0.49 vs. r = 0.61-0.68 for the others). Women demonstrated digit preference for the 15th, 1st, 20th, or 5th of the month in reporting LMP dates, with 22% reporting those dates vs. 13% expected. The deviation between actual and predicted date of delivery among term births was calculated, assuming the pregnancy should have ended 280 days after the LMP. The interval ±2 weeks included 80% of births based on LMP vs. 87-88% for US or US + LMP. The main disparity was in the fraction of births for which the actual date of delivery was later than predicted: 11% of LMP estimates were 2+ weeks earlier than delivery vs. 2.6–3.5% of US or US + LMP estimates. A sizable fraction of LMP estimates appear to be in error, with actual duration of gestation notably longer than predicted, and those errors are correctable by US.

#### Pregnancy-associated injury hospitalizations: maternal and fetal outcomes

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Background. Although injury is one of the leading causes of morbidity and mortality among reproductive-aged women, relatively little research has focused on pregnant women. The purpose of this study was to determine the incidence rate, causes, and outcomes of pregnancy-associated injury hospitalizations in Washington. Methods. A retrospective cohort design was used to evaluate women hospitalized for injury during pregnancy in Washington State from 1989 to 1997. Pregnant women hospitalized for injury were identified by linking Washington state files containing birth and fetal death certificate data with hospital discharge data from all Washington state civilian hospitals, with injury defined as any ICD-9 injury diagnosis or external causation codes except poisonings and medical misadventures. These women were compared with a randomly chosen group of delivering women not experiencing an injury hospitalization during pregnancy. Pregnancy outcomes were evaluated using relative risks (RR) and 95% confidence intervals (95% CI). Results. The overall incidence of pregnancyassociated injury hospitalizations was 243.4/100000 live births. Motor vehicle crashes (30.4%), falls (27.3%), and assaults (8.2%) were the most common causes of injuries. Pregnant women hospitalized for injury were at increased risk of placental abruption (RR 3.3, 95%CI 2.5-4.3), cesarean delivery (RR 1.2, 95%CI 1.1-1.3), and death (RR = 11.5, 95%CI 1.9-68.7) compared with non-injured pregnant women. Their infants were at increased risk of low birth weight (<2500 g) (RR 2.0, 95%CI 1.6-2.3), prematurity (<37 weeks) (RR 1.8, 95%CI 1.5-2.0), and fetal death (RR 2.2, 95%CI 1.2-4.0) compared with infants of non-injured women. Conclusion. The high incidence of injuries among pregnant women leads to significant morbidity.

#### The sex ratio of pregnancies complicated by hyperemesis gravidarum

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Background. Observational studies of women with pregnancies complicated by hyperemesis gravidarum (HG) have demonstrated elevated estrogen levels as well as a high infant female to male sex ratio. Hyperemesis gravidarum may be a marker for high estrogen levels in utero associated with the subsequent development of hormonally sensitive cancers in offspring. Methods. The infant sex ratio for pregnant women admitted to the hospital for HG in Washington State was evaluated in a population-based case control study of 11 893 women. This study utilized the Comprehensive Hospital Abstract Reporting System linked to the Birth Certificate System for the calendar years 1987–96. Cases (n = 2110) included all women hospitalized for HG in the first trimester of pregnancy who subsequently had a live birth. Controls (n = 9783) were women who experienced a live birth during the same time period but were not hospitalized for HG. Results. Women with HG had a 50% increased chance of having a female infant compared with controls (Odds Ratio 1.5, 95% Confidence Interval 1.4-1.7). Women with severe HG, as measured by hospitalization for 3 or more days, had an even greater likelihood of having a female infant compared with control women (Odds Ratio 1.8, 95% Confidence Interval 1.6-2.1). Conclusions. Hyperemesis gravidarum is associated with a preponderance of female live births. Additional studies are needed to compare hormone levels in hyperemesis gravidarum and normal pregnancies and evaluate the hypothesized association of altered in utero hormone levels with subsequent risk of hormonally sensitive cancers in later life.

### Insulin-like growth factor-1 is associated with gestational weight gain and preterm delivery

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Insulin-like growth factor-1 (IGF-1) increases during pregnancy, particularly during the third trimester when it is produced by the placenta and thought to regulate the nutrient flux from mother to fetus. Alterations in the production of maternal IGF-1 thus may be a risk factor/marker for a compromised pregnancy. The authors examined the influence of IGF-1 during gestation in 795 gravidas from Camden. Throughout pregnancy, IGF-1 bore a striking relationship with gestational weight gain. For example, at entry (14.6  $\pm$  7.9 week) low levels (10th percentile) predicted an increased risk of inadequate weight gain for the whole of gestation (Adjusted Odds Ratio [AOR] = 1.80, 95% Confidence Interval [CI] 1.04-3.11) while high levels (90th percentile) predicted decreased risk (AOR = 0.33, 95% CI 0.15–0.77). At week 28, but not entry, low IGF-1 (10th percentile) was associated with shortened gestation ( $-0.78 \pm 0.33$  weeks, P < 0.01), a tenfold increased risk of very preterm delivery (AOR = 10.26, 95% CI 1.77-59.41) and a twofold increased risk of preterm delivery (AOR = 2.78, 95% CI 1.01-7.63). Low maternal IGF-1 at week 28 resulted from the failure of IGF-1 to rise from

baseline ( $0.69 \pm 2.57 \,\text{ng/mL}$  [low IGF-1] vs.  $104.24 \pm 7.06 \,\text{ng/mL}$ , P < 0.001). For comparison, the rise in IGF-1 was reduced by more than 85% with very preterm delivery (P < 0.01) and by more than 50% with preterm delivery (P < 0.05). These data are the first to suggest that low maternal IGF-1 (likely impaired placental production) is a risk factor/marker for preterm delivery. Further, the controversial relationship between inadequate gestational gain and preterm delivery may reflect low maternal IGF-1.

#### Risk factors for Attention Deficit Hyperactivity Disorder among school-aged children in Iran

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Objective. We examined the association between pregnancy, delivery, and infancy complications (PDICs) with Attention Deficit Hyperactivity Disorder (ADHD) among school-aged children in Iran. Methods. In this retrospective matched casecontrol survey, a multistage sampling technique was used to select 84 elementary school students (six to 11-year-old-children) who met the DSM-III-R criteria for ADHD from 16 schools in four educational regions in Tehran. These cases were matched to 84 other students according to their age, sex, and family socioeconomic status (N = 168). For each child, information on PDICs was obtained from his/her biological mother in a standardized manner blind to the child's status. Results. McNemar's test for paired qualitative data revealed significant differences between the two groups for some of the factors including taking unprescribed medications during pregnancy ( $\chi^2 = 5.04$ , d.f. = 1, p < 0.025), hypoxemia at birth ( $\chi^2 = 5.82$ , d.f. = 1, p < 0.025), long labour ( $\chi^2 = 4.76$ , d.f. = 1, p < 0.05), and history of head injury  $(\chi^2 = 9.48, d.f. = 1, p < 0.005)$ . Logistic regression found long labour (OR = 22, 95% CI = 2.0–228.5) and head injury (OR = 32, 95% CI = 3.5–293.7) to be significant. **Conclusion.** As the first analytical study in the area of school-aged children's behavioralemotional disorders within the unique Iranian social and cultural context, this study underscores the importance of mental health education and other preventive programs for ADHD.

## Is there an association between maternal folate status in the second trimester and preterm birth?

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Poor maternal folate status during pregnancy has been suggestive of an increase in preterm birth. The goal of this study was to assess the association between folate status (serum, red blood cell, and dietary intake) during the second trimester of pregnancy and preterm birth, controlling for potential confounders. Data were obtained from the Pregnancy, Infection, and Nutrition Study from 1995 through 1998. Women who were recruited into the study at

24-29 weeks gestation provided a blood sample and completed a food frequency and sociodemographic/health behavior questionnaire. Both serum (n = 1825) and red blood cell (n = 887) folate were analyzed using immunoassay techniques. Dietary folate was poorly correlated with serum (r = -0.08) and red blood cell (-0.05) folate, even after accounting for supplement use. Serum folate was moderately associated with red blood cell folate r = 0.43. The lowest tertile of serum folate was consistently associated with preterm birth even after adjustment for supplement use, smoking, and pregravid BMI (AOR = 2.0, 95% CI = 1.4, 2.8), with a stronger association among non-supplement users (AOR = 2.9, 95% CI = 1.2, 7.3). There was no association with dietary intake. The unadjusted odds ratio for the lowest tertile of red cell folate was near the null for the entire sample as well as for supplement users, but was 1.56 (95% CI = 0.8, 2.8) among non-supplement users. The adjusted odds ratio was 1.24 (95% CI = 0.84, 1.8) for the entire sample, which did not change much after stratification by supplement use (AOR = 1.24 supplement vs. 1.39 non-supplement users). Serum folate was associated with a preterm birth when measured in the second trimester of pregnancy, but the discordant results between the short (serum) and long (red blood cell) term markers of folate status and preterm birth warrant further investigation.

#### Young maternal age and poor pregnancy outcomes: revisiting the association

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The association between young maternal age and poor pregnancy outcomes remains controversial. Some studies have found that giving birth before the age of 20 increases the risk of low birth weight (LBW), preterm birth (PTB) or intrauterine growth retardation (IUGR) whereas others did not identify such associations. In most studies, associations tend to disappear after controlling for socioeconomic and reproductive factors, thus indicating that social disadvantage rather than biological factors may explain them. The relation between young maternal age and poor pregnancy outcomes was studied in North-east Brazil, where the prevalence of teenage pregnancy was 29%. A systematic sampling of 2436 hospital births, stratified by hospital, was performed in São Luís, North-east Brazil, from March 1997 to February 1998. The risks of young mothers having LBW, PTB or IUGR were calculated, with and without adjustment for socioeconomic or reproductive factors in a logistic regression model. LBW rate was 7.2%, PTB rate was 12.7% and the prevalence of IUGR was 14.2%. In the unadjusted analysis, the risks of LBW, PTB or IUGR were higher for mothers younger than 18 years, but not for those aged 18 or 19 years. After adjustment, the risks of LBW or IUGR associated with young maternal age (<18) were no longer significant, whereas the risk of PTB remained significant after controlling for socioeconomic and reproductive variables. The increased risks of LBW and IUGR seem to be mediated by socioeconomic and reproductive factors. However, the high risk of PTB for mothers younger than 18 years might have a biological or artifactual explanation.

#### Infant feeding practices among mothers of very low birth weight (VLBW) infants

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Background. Breastfeeding is the optimal feeding method for all infants. Mothers of VLBW infants face additional obstacles to achieve successful breastfeeding. This study examines factors that predict expressed milk and breast feeding practices among mothers of VLBW infants. Methods. The sample consists of 347 children, enrolled in a follow-up study of the Developmental Epidemiology Network (DEN) cohort that included infants <1500 g born in four hospitals between 1991 and 1993. Information regarding infant feeding practices and sociodemographic factors were obtained from maternal interview at follow-up. Chart review at birth provided data on neonatal characteristics. Results. In this study, 57.0% of mothers reported providing expressed human milk feedings. Of these, 29% of mothers (16% of the entire cohort) reported directly breast feeding their infants. The duration of human milk feedings was brief with a median duration of 1-3 months. Higher maternal verbal IQ and social class scores positively influenced the decision to initiate expressed milk feedings. Higher values for infant birth weight and gestational age, social class status and maternal age supported the transition from expressed milk feedings to direct breast feedings while extended hospitalization decreased the likelihood of direct breast feedings. Conclusions. These results indicate that different sociodemographic factors and infant characteristics affect the feeding practices of VLBW infants. The low prevalence of breastfeeding among VLBW infants highlights the need to promote human milk feedings among these high-risk infants.

#### Lead (Pb) in breast milk and maternal bone turnover

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Lead (Pb) concentrations in breast milk could arise from the liberation of heavy metals from their bone 'sink' during the substantial bone turnover in reproduction, including lactation. The authors related Pb breast milk to maternal blood Pb and to osteocalcin (a measure of bone turnover) in 15 women who had been lactating at least 3 months. Data were collected at delivery, 3 months, and 6 months. Pb in breast milk was determined by Isotope Dilution Inductively Coupled Plasma Mass Spectrometry, while maternal blood Pb concentrations and osteocalcin were measured by atomic absorption spectrophotometry and radioimmunoassay, respectively. Bone mineral density (BMD) was assessed by dual energy X-ray absorptiometry. Pb breast milk concentrations were 6.2, 6.2, and 5.5 ppt at delivery, 3 and 6 months postpartum, respectively, which is significantly different from zero (P < 0.0001). Maternal blood Pb concentrations were 1.3, 1.6 and 1.5 mg/dL in the same time frame. Mean

maternal blood Pb concentrations were approximately 4 times greater than mean breast milk Pb but maternal and breast milk Pb values from the same time were not correlated with each other. Breast milk Pb was not correlated to absolute osteocalcin concentrations, change in osteocalcin concentrations or change in BMD, though the sample size was very small. This study indicated that breast milk Pb concentrations were approximately 25% of the average maternal blood Pb and that the mean breast milk value was as high at delivery as it was following 3 months of lactation. Lead in breast milk could not be linked to greater bone turnover in lactation.

## The associations between insulin-like growth factor-1, bone turnover and bone loss in HIP/toxemia

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Hypertension of pregnancy (HIP)/toxemia, a pregnancy disorder of uncertain etiology, affects 5-10% of all pregnancies. The authors hypothesized that contributors to calcium metabolism including IGF-1, osteocalcin (a marker of bone turnover), and bone loss would be different among women with HIP/toxemia compared with normotensive pregnant women. 1052 healthy women, aged 12-35, were recruited at the first prenatal visit and assessed in each trimester and at delivery for osteocalcin and IGF-1 concentrations. Bone ultrasound was measured at entry to care and at 6 weeks postpartum. Seven percent of women developed HIP/toxemia. There were different relationships between IGF-1 and osteocalcin concentrations during pregnancy in women who had PIH/toxemia as compared with normotensive pregnant women. In normotensive women, there was no increase in IGF-1 concentrations in the second trimester and a modest increase (~33%) in the third trimester while osteocalcin concentrations dropped by 60%. In women with HIP/toxemia, IGF-1 concentrations were 40% and 70% greater in the second and third trimesters, respectively, with little change in osteocalcin concentrations. These changes were associated (r = 0.80) with greater bone loss among women with HIP/toxemia. Among women with HIP/toxemia, there was a greater likelihood of bone loss by ultrasound and relative non-responsiveness of osteocalcin concentrations to greater IGF-1 compared with normotensive women who demonstrated less likelihood of bone loss and less bone turnover, assessed with osteocalcin.

#### Trends and racial differences in the prevalence of and mortality from congenital diaphragmatic hernia (CDH)

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**Objective.** The authors compared the prevalence of and mortality from CDH by race in US for the years 1989–91 and 1995–97. **Design/methods.** The data for the study was derived from the

US linked birth and infant death data. The study population consisted of all infants born to White and African-American (AA) mothers (N = 22780585). We compared the prevalence of and mortality from CDH by race between two periods (Period I: 1989-91; Period II: 1995-97). Logistic regression was used for the risk of prevalence and mortality. Results. There was no difference in the prevalence of CDH between the Periods I and II (adjusted odds ratio [OR] 0.96; 95% CI, 0.89-1.03). The prevalence of CDH was 43% less frequent in AA infants compared with White infants (adjusted OR 0.57; 95% CI, 0.50-0.64). CDH was 23% less frequent in female infants compared with male infants (adjusted OR 0.77; 95% CI, 0.71-0.83). CDH-specific neonatal mortality rate was different neither between the two Periods (adjusted OR 1.01; 95% CI, 0.86–1.20), nor between AA and White infants (adjusted OR 0.93; 95% CI, 0.72-1.20). However, there was 24% reduction in non-CDH neonatal mortality rate between these two Periods (adjusted OR 0.76; 95% CI, 0.75-0.77). Conclusions. Prevalence of CDH has not changed in the last decade. The prevalence of CDH was significantly less in AA infants and in female infants. There was no change in CDH-specific neonatal mortality rate in the last decade, while neonatal mortality from other disorders was significantly reduced.

#### The association of bacterial vaginosis, smoking, and race in an obstetric population

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Background. Both maternal smoking and bacterial vaginosis (BV) have been associated with an increased risk of preterm delivery and preterm premature rupture of the membranes. Black women have a two- to three-fold increased risk for colonization with BV compared with white women, while having a lower rate of smoking. The objective of this secondary analysis was to examine in a pregnant population the interrelationship between smoking, race, and the presence of BV. Methods. All singleton pregnancies from the Preterm Prediction Study (n = 2929) and the Home Uterine Activity Monitoring Prediction Study (n = 454) who were not lost to follow-up were included in the analysis. Smoking was defined as smoking at any time during the pregnancy. BV was defined as a Gram Stain score >7. Chi-square test was used for univariate analysis, with Mantel-Haenzel stratification by race. The dose-response relationship between BV and number of cigarettes smoked was also assessed. Results. The unadjusted relative risk did not support an association between smoking and Gram Stain score >7 (RR = 0.91, 0.81-1.01, p = 0.081). When stratified by race, smoking was associated with a Gram Stain score >7 (RR = 1.15, 1.02–1.28, p = 0.019). Within the subgroups, smoking and Gram Stain score were associated among non-blacks (RR = 1.27, 1.01-1.59), but not among blacks (RR = 1.10, 0.96-1.25). A non-significant trend of increased rate of BV with an increasing number of cigarettes smoked was present among non-blacks, but not among blacks. Comment. While an association between smoking and BV is not present in the overall

study population, an association that is more pronounced in nonblacks is present with stratification by race. This analysis suggests there are racial differences in the unidentified mechanism linking BV and smoking.

#### Methods to recruit an ethnically diverse cohort of pregnant women from WIC

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Large ethnic disparities exist in the risk of adverse birth outcomes. However, recruitment of ethnically diverse pregnant women into cohort studies remains a challenge. A pilot study was conducted to recruit and follow pregnant women attending six Women, Infants, and Children (WIC) clinics in the Twin Cities. Three interviews were conducted: one in-person (second trimester) and two by telephone (late in pregnancy, one month postpartum). Blood samples were obtained at initial interview. Following birth, neonatal blood spots were retrieved from the Minnesota Department of Health. Of 159 pregnant women described in the study by WIC staff during a six-month period, 107 (67%) were successfully recruited. An active method that involved WIC staff and provided three participant incentives was the most effective of three recruitment methods tested. Racial/ethnic demographics of the cohort (42 white, 33 African-American, 18 Hispanic, and 14 other ethnicities) were not statistically different from the underlying distribution of women seen at the clinics (P = 0.50). Blood samples were obtained from 101 (94%) women. While only 64 (60%) of the women were located for the third trimester interview, with additional time for tracking methods, all 107 women were located for the final postpartum interview. Of the 99 (93%) women who gave birth in Minnesota, all neonatal blood spots were successfully retrieved from the Health Department. This pilot study demonstrates the feasibility of recruiting and following an ethnically diverse pregnant population and collecting blood samples from both mother and infant for hypothesis testing related to adverse birth outcomes.

### Spontaneous abortion and assisted reproductive technology in the United States

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Surveys of women undergoing assisted reproductive technology frequently note an increased rate of spontaneous abortion. Using population-based data of assisted reproductive technology procedures performed in United States clinics, the authors examined the rate of spontaneous abortion and associations of various factors with spontaneous abortion for clinical pregnancies resulting from assisted reproductive technology procedures initiated in 1996 and 1997. The authors defined clinical pregnancy as the presence of one or more gestational sacs observed via ultrasound. Classification of spontaneous abortion was based on

provider report of a spontaneous abortion and was defined as loss of the entire pregnancy (does not include a reduction in the number of fetuses in a multiple-gestation pregnancy). Over 96% of spontaneous abortions with timing data occurred at less than 20 weeks of gestation. A total of 5448 spontaneous abortions occurred among 39 101 clinical pregnancies. This overall rate of 13.9 spontaneous abortions per 100 clinical pregnancies is not greater than an expected rate (based on published reports) of approximately 10-15 spontaneous abortions per 100 clinically recognized spontaneous pregnancies. Spontaneous abortion risk increased significantly with increasing age, previous miscarriages, previous attempts at assisted reproductive technology, and use of embryos that had been frozen. The risk of spontaneous abortion decreased significantly with pregnancy plurality between 2 and 5 fetuses compared with 1 fetus, use of oocytes from a woman serving as an egg donor, and availability of extra embryos (a marker for patient response to treatment and embryo quality). The findings provide insight into the occurrence of spontaneous abortion in pregnancies resulting from assisted reproductive technology.

#### Pregnancy-intendedness and lifestyle factors: is there a relation?

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Unintended pregnancies account for about 49% of pregnancies in the United States. Poor pregnancy outcomes (i.e. low birth weight, birth defects) are associated with behaviors (i.e. alcohol use, smoking) that may be more common among women whose pregnancy was unintended. Whether pregnancy intendedness is associated with such behaviors is unclear. The authors evaluated the relation between intention to become pregnant and prenatal alcohol, smoking, and vitamin use, based on data from 3029 mothers who gave birth to infants without birth defects from 1968 to 80 and who were interviewed in 1982-83. Pregnancy intention, alcohol use, cigarette smoking, and vitamin use were defined from maternal self-reports. Women with unintended pregnancies were younger, non-White, less educated, and had higher parity (all p < 0.001). Since most women would be aware of their pregnancies by the end of the first trimester, exposure in the third month of pregnancy was used for the analysis of alcohol and smoking. After adjusting for maternal race, age, education, and parity, women with unintended pregnancies were more likely to report smoking (odds ratio [OR] = 1.3, 95% confidence interval [CI] 1.1-1.6) than women with intended pregnancies, but no association was observed between pregnancy intention and alcohol use (OR = 1.1, 95% CI 0.9–1.3). Unintended pregnancy was associated with not taking vitamins preconceptionally or in the first trimester (OR = 1.4, 95% CI 1.2-1.7). These results suggest that unintended pregnancies are associated with some exposures that may result in adverse pregnancy outcomes, and that some prevention efforts should specifically target this at-risk population.

#### Trends in postneonatal mortality in the United States, 1988–98

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Background. Postneonatal mortality (PNM), deaths among infants 28-364 days, is frequently preventable. Examining trends in PNM can assist in prioritizing prevention strategies and targeting high-risk populations. Methods. The authors used US infant death certificate data to analyze trends in PNM during 1988-98. Postneonatal mortality rates per 1000 live births were examined by race and region of residence. Rate ratios between black and white infants were calculated. The leading causes of PNM were evaluated and trends compared over time. Results. Postneonatal mortality, which accounts for one third of all infant mortality, declined 34.1% from 3.6 in 1988 to 2.4 in 1998 (36.1% decline among white and 26.7% among black infants). A decrease in deaths due to sudden infant death syndrome (SIDS) accounted for most of the decline. During the study period, the overall black-towhite rate ratio increased from 2.1 to 2.4. Regionally, racial disparities in PNM rates widened, except in the South were the black-to-white ratio remained relatively stable and consistently lower than in other regions. Overall, SIDS remained the leading cause of PNM in 1998 (27.9% of all deaths), followed by congenital anomalies (18.2%), infections (12.3%), injuries (10.7%), and perinatal conditions (6.8%). All five leading causes of PNM declined over the study period. The overall PNM rate due to injury declined least while the PNM rate attributable to intentional injury increased by 7.9% from a 10-year low in 1988. Conclusions. Approximately half of all PNM is caused by potentially preventable outcomes, such as SIDS, infections and injuries. While the overall PNM rate declined, intentional injury rates increased and racial disparities persist. Interventions targeted toward highrisk groups may help reduce PNM and eliminate racial disparities.

#### Why do North African immigrants in Belgium have high birthweight infants?

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Infants of North African immigrants are reported to have higher birthweights than their Belgian counterparts, despite their lower socioeconomic status. However, it remains unclear what mechanism contributes to this difference, as Belgian birth certificate data offer limited information. In order to study this association further, the authors conducted a hospital-based study of 1189 pregnant women attending public prenatal care clinics in 3 Belgian hospitals between May 1994 and April 1995. Women with multiple pregnancies and those whose pregnancies resulted in a stillbirth were excluded. North African status was based on the nationality at birth and included Moroccan, Tunisian, and Algerian women. Three hundred and sixty-one North African and 828 Belgian women were included in the study. Mean birth-

weight was identified as 3182 g among Belgian and 3343 g among North African infants, a 161-g difference (P < 0.01). North African women were more likely to be older, multiparous, and to have high prepregnancy weight, while Belgian women were taller and were more likely to smoke. After adjusting for maternal age, parity, prepregnancy weight, maternal height, and cigarette use, the birthweight difference was reduced to 60 g (P = 0.09). The authors concluded that the higher birthweights observed among infants of North African immigrants were partly explained by differences in smoking, body mass, or sociodemographic factors.

### Risk factors for acute otitis media in young infants with special attention to race

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Acute otitis media (AOM) results in over 20 million office visits per year in the US and is the most common reason for antibiotic use among children. AOM in the first six months of life increases the risk of recurrent AOM and chronic otitis media with effusion. The association between AOM and race has been unclear from previous research. The authors analyzed data from 11 349 sixmonth-old infants in the Infant Care Practices Survey, a longitudinal cohort study conducted in 1995-8. Multivariate logistic regression analysis adjusting for a variety of potential confounders demonstrated a lower risk of AOM among Black infants compared with White infants (OR = 0.75, 95%CI 0.62-0.90), with intermediate risk for Asian infants (OR = 0.80, 95%CI 0.59-1.1) and Hispanic infants (OR = 0.90, 95%CI 0.73-1.1). AOM was also associated with the following factors: male sex (OR = 1.1, 95%CI 1.0-1.2), out-of-home daycare (with increasing OR's for larger daycare centers; 1-3 children: OR = 1.5, 95%CI 1.2-1.8; 4-6 children: OR = 2.0, 95%CI 1.7-2.3; 7-12 children: OR = 2.9, 95%CI 2.3-3.5; >12 children: OR = 3.7, 95%CI 2.5-5.5), number of children living in the home (2 children: OR = 1.5, 95%CI 1.3-1.6; 3 children: OR = 1.5, 95%CI 1.3-1.7; 4 or more children: OR = 1.9,95%CI 1.6-2.3), unmarried mother (OR = 1.2, 95%CI 1.0-1.4), breastfeeding (OR = 0.69, 95%CI 0.61–0.78), and older maternal age (>34 years: OR = 0.81, 95%CI 0.70–0.93, compared with 25–34 years). Factors not associated with AOM included pacifier use, exposure to cigarette smoke, maternal smoking during pregnancy, household income, mother's education level, household crowding, and number of adults living in the home. These findings suggest that even when socioeconomic status, living conditions, and infant care practices are taken into account, Black infants have a lower risk of AOM than White infants.

### Association of early infant exposures to wheezing and asthma by age five

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It has been suggested that asthma in young children may be associated with exposures during infancy. The authors examined pos-

sible associations between exposures during the first 6 months of life and wheezing or diagnosis of asthma reported by age 5 among 790 term infants enrolled at birth and whose parents completed questionnaires at 1, 3, and 6 months and 5 years of age. Multiple logistic regression analysis was used to calculate odds ratios (OR) and 95% confidence intervals (CI). Models included independent variables obtained during the first 6 months of life: maternal age, race/ethnicity, marital status, education, income, parity, breastfeeding, and infant sex, sleep position, pacifier use, tobacco smoke exposure, and medical visits for OM, respiratory illness, or vomiting/spitting up. Wheezing or asthma was reported in 24% of children by age 5. After controlling for all other factors, children having had a medical visit for a respiratory problem (OR = 4.4, 95%CI = 2.6–7.6) or exposed to environmental tobacco smoke (OR = 1.7, 95%CI = 1.0-3.0) in the first 6 months of life were more likely to report wheezing or asthma by age 5. Children of single mothers (OR = 2.2, 95%CI = 1.1-4.2) and mothers who reported using asthma medications after the birth of their children (OR = 3.1, 95%CI = 1.1-9.2) were also at increased risk of wheezing or asthma. Several factors identified in early infancy appear to be associated with reported wheezing or asthma by age 5 including respiratory problems requiring medical visits, maternal marital status and use of asthma medications, and exposure to tobacco smoke. (Supported by NICHD N01 HD43221 and NHLBI HL62371)

#### Effect of poverty on mortality risk during the postneonatal period in VLBW infants

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Risk of postneonatal mortality is increased by poverty and by chronic medical conditions secondary to extreme prematurity. The authors investigated whether, during the postneonatal period, the mortality risk associated with poverty is greater for VLBW than for normal birth weight (NBW; 2500 g–4000 g) infants. IL-linked birth-death certificates from 1989 to 96 for Chicago mothers were merged to 1990 US census tract data on median household income (MHI). The mortality risk associated with MHI >\$15 000, adjusted for birth weight and race, was calculated using logistic regression for clustered data. We compared the poverty-associated mortality risk for VLBW and NBW infants at the following postneonatal ages: 28 days, 3 months, 6 months, and 9 months. Mortality odds ratios (OR, 95% CI) associated with poverty are shown for death after 28 days, 3 months, 6 months,

Death			
after	VLBW	NBW OR	Ratio
28 days	1.23 (1.0, 1.5)	1.25 (1.2, 1.3)	1.0
3 month	1.35 (1.1, 1.7)	1.37 (1.3, 1.5)	1.0
6 month	1.80 (1.4, 2.4)	1.20 (1.1, 1.3)	1.5
9 month	2.80 (2.0, 4.0)	1.00 (0.9, 1.1)	2.9

and 9 months. The last column is the VLBW:NBW ratio of the OR for each postneonatal age group.

Mortality risk associated with poverty in the postneonatal period becomes progressively greater for VLBW than for NBW infant over the second half of the first year of life, likely reflecting VLBWs increased vulnerability to the effects of poverty following hospital discharge. Research aimed to understand and reduce the adverse health effects of poverty in VLBW infants is critical to improving their long-term survival.

### Multiple births among women who took folic acid during early pregnancy – Sino–US NTD Project

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Folic acid (FA) supplements are recommended for women of childbearing age to prevent neural tube defects (NTDs). Two recent articles have reported an increased risk of multiple births (MB) among women who took vitamins or FA during early pregnancy. The authors evaluated the occurrence of MB in a cohort of women who had participated in a campaign in China to prevent NTDs with daily FA pills (400 µg/day). The authors excluded all birth defect-affected births. FA use was ascertained before pregnancy outcome was known. For each of three time periods when use of FA could have the potential to influence the rates of monozygotic and dizygotic twinning (prior to ovulation, during fertilization, and after conception), the authors used records of FA pill use to classify women into three pill-taking patterns (full exposure, partial exposure, or no exposure). The authors compared rates of MB during each of these periods according to a woman's use of FA. Among 242015 women, the authors identified 1509 (0.6%) MB; the overall rate among women who took any FA was 0.6% and among women who did not take FA was 0.7% (Risk ratio [RR], 0.90; 95% confidence intervals [CI] 0.82-1.00). Among women who were taking FA prior to ovulation, during the time of fertilization, and after conception, the rates of MB were 0.6% (RR, 0.89; 95% CI, 0.79–1.00), 0.6% (RR, 0.88; 95% CI, 0.78–0.99) and 0.6% (RR, 0.89; 95% CI, 0.77–1.02), respectively. Women with partial FA exposure had risks similar to those of women with full exposure in each group; in all cases, the risk of MB among FA users was lower than among nonusers. In this population-based evaluation, the authors found no evidence that maternal consumption of FA before and during early pregnancy increases the occurrence of MB.

#### Maternal obesity and abdominal wall defects

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Little is known about risk factors for abdominal wall defects (AWD). Because studies have found higher risks for neural tube defects among infants of obese women, the authors examined the relation between self-reported maternal prepregnancy body mass

index (BMI) (kg/m<sup>2</sup>) and AWD in infants born during 1993-96 in Atlanta to underweight (BMI < 18.5), average weight (BMI 18.5–24.9), overweight (BMI 25–29.9), and obese women (BMI ≥ 30). Included were 19 infants with nonsyndromic omphalocele, 23 infants with gastroschisis, and 340 infants born without birth defects. After adjusting for maternal age, the authors found that obese women were more likely than average-weight women to have an infant with omphalocele (odds ratio [OR] = 4.0, 95% confidence interval [CI] 1.3-12.1). Six (32%) of 19 mothers of infants with omphalocele but none of the 23 mothers of infants with gastroschisis were obese. Adjusting for several other possible confounders had little effect on the risk estimate for omphalocele (OR = 3.6, 95% CI 1.1–11.7). The OR for omphalocele was 0.6 (95% CI 0.1-4.8) for underweight women and 1.2 (95% CI 0.3-4.9) for overweight women. The OR for gastroschisis was 0.4 (95% CI 0.1-3.3) for underweight and 1.4 (95% CI 0.5-4.0) for overweight women. The obesity-related risk for omphalocele was higher for infants with omphalocele occurring with other defects (crude OR = 8.9, 95% CI 1.4-55.0) than for those with isolated omphalocele (crude OR = 2.5, 95% CI 0.6-10.3). This small study found a relation between maternal obesity and omphalocele but not gastroschisis. This is consistent with the etiologic heterogeneity suggested for these two defects. If other studies confirm this relation, it is of concern, especially given increasing obesity prevalence among women.

#### The impact of missing birthweight on comparison of birthweight-specific mortality

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Studies on the potential impact of missing birthweight information on the comparison of birthweight-specific feto-infant mortality rates have been sparse in literature. The authors used data collected from two nationwide surveys of all gestational outcomes occurring 15-17 May 1989 and 12-16 February 1996, respectively, in Taiwan and the 1989 and 1996 linked birth and infant death records in Canada (excluding Ontario and Newfoundland) to address this issue. Fetal and infant mortality rates in the overall study sample and three subsamples were calculated and compared: (1) births with missing birthweight information; (2) births with weight <500 g; and (3) excluding births with birthweight either missing or <500 g, and fetal, neonatal, and postneonatal mortality among births with birthweight of 500–1499 g, 1500–2499 g, and ≥2500 g in Taiwan and Canada. Relative risks and 95% confidence intervals were used for all comparisons, with Canada as the reference. The results showed that fetal and infant mortality rates were only moderately higher in Taiwan than in Canada in the overall study sample comparison. Infant and (especially) fetal death rates were substantially higher in Taiwan than in Canada among births with missing birthweight but substantially lower in infants with birthweight <500 g. In other birthweight groups, fetal death rates were lower and infant death rates were slightly higher in Taiwan than in Canada. The authors conclude that differences in missing birthweight information between deaths and survivors can bias comparisons of birthweight-specific feto-infant mortality.

#### The effect of binge drinking near conception on the risk of small-for-gestational-age birth

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Binge drinking during pregnancy has been associated with developmental changes in infant EEGs and decreased infant head circumference, but a study of occasional binge drinking among moderate drinkers found no association with mean birth weight, length, head circumference, gestational age, or intrauterine growth retardation. The authors studied the effect of binge drinking in the 3 months prior to pregnancy on the risk of a singleton, term, small-for-gestational-age birth. Study data were from the Pregnancy Risk Assessment Monitoring System, an ongoing study that collects data from a state population-based sample of women who delivered a live born infant 2-6 months previously. The sample is drawn from state birth certificates and data are collected by mailed questionnaires with phone follow-up. The analysis used births in 17 states from 1995 to 1999. Logistic regression was used to model the association between patterns of alcohol use and small-for-gestational-age birth while controlling for characteristics associated with binge drinking. 13.4% of the represented population binge drank at least once in the 3 months before they became pregnant. Almost 90% of binge drinkers drank, on average, less than 7 drinks/week. Binge drinking did not increase the risk of small-for-gestational-age birth (OR: 0.9 [0.8, 1.0]) or among women who averaged <7 drinks/week (OR: 1.0 [0.9, 1.1]). Among moderate and heavy drinkers, however, binge drinkers had almost twice (OR: 1.9 [1.0, 3.7]) the risk of a small-for-gestational-age birth compared with those who did not binge. Binge drinking around the time of conception appears to increase the risk of small-for-gestational-age birth only among women who drink at least 7 drinks/week.

#### Pregnancy-related mortality due to cardiomyopathy: United States, 1991–97

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Cardiomyopathy accounts for an increasing proportion of pregnancy-related deaths in the United States. These deaths include those due to peripartum cardiomyopathy, a poorly understood condition in women with no previous history of cardiac disease; and those from secondary and pre-existing cardiomyopathy. This paper describes pregnancy-related mortality due to cardiomyopathy and its attendant risk factors in the US from 1991 to 1997. The authors used data from the CDC's Pregnancy Mortality Surveillance System, which is based on death certificates and matching birth and fetal death certificates. A pregnancy-related death was defined as the death of a woman during or within one year of pregnancy caused by pregnancy, its treatment or complications. Pregnancy-related mortality ratios (PRMR) were defined as the number of pregnancy-related deaths per 100 000 live births. From 1991 to 1997, there were 245

pregnancy-related deaths due to cardiomyopathy in the United States, accounting for 7.6% of all pregnancy-related deaths, compared with 3% in 1979–84. Of these, 73% were due to peripartum cardiomyopathy, and 27% to secondary or pre-existing cardiomyopathy. The PRMR due to cardiomyopathy was 6.4 times higher for black women than for white women. Almost half the cardiomyopathy deaths occurred after 42 days postpartum. Cardiomyopathy is a rare but increasingly recognized complication of pregnancy. The rising number of reported deaths may be due to improved case ascertainment by using the definition of pregnancy-related mortality that extends to 1 years postpartum, as opposed to 42 days. Preventing these deaths will require a better understanding of the risk factors for and etiology of peripartum cardiomyopathy.

#### Factors associated with the sex ratio at birth

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The ratio of male to female births and its purported decline has received increased attention in environmental health as a potential marker of exogenous effects on development, particularly of hormonally active compounds. We used data from a large prospective study of pregnant women during the 1960s to examine the sex ratio by a variety of prenatal factors in order to better understand its inherent variability. We limited the analyses to one livebirth per woman, yielding 6151 males and 5943 females (% male is 50.86). The male proportion was decreased among infants with younger mothers (47.79%) or fathers (45.85%), or with a greater parental age difference. It was significantly increased with higher maternal (51.72%) or paternal (52.51%) education. By race, Blacks and American-Indians tended to have fewer male births and Asians had more (55.5%) than Whites. Other associations found were a winter conception (male odds ratio (OR) = 1.10, 95% CI 1.01-1.19) and prior multiple birth (male OR = 1.71, CI 1.08-2.71). Most of these associations were similar after adjustment for covariates. In the logistic regression models, maternal smoking was also associated with more male births (OR = 1.08, CI 0.99-1.18), but paternal smoking was not. A number of other factors, such as gravidity, income, prepregnancy weight, and caffeine or alcohol consumption, showed little association with the sex ratio. For others (cycle length, contraception, age at menarche), small subgroups limited the power for detecting an effect. The results offer some support for hormonal mechanisms, but indicate the difficulty of identifying environmental hazards due to the large sample sizes needed.

### The impact of pregnancy-induced hypertension on birth weight by gestational age

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The predominant etiological theory of preeclampsia is that reduced uteroplacental perfusion is the primary step and the point of convergence of diverse pathogenic processes in the development of preeclampsia. Decreased uteroplacental blood flow should result in lower birth weights. No study to date has assessed the effect of preeclampsia and gestational hypertension on birth weight by gestational age. To study the impact of preeclampsia and gestational hypertension on birth weight according to gestational age, we conducted a retrospective cohort study based on 97 270 pregnancies delivered between 1991 and 1996 in 35 hospitals in Northern and Central Alberta of Canada. Analysis of variance and multivariable linear regression were performed to compare the mean birth weights of babies born to mothers with gestational hypertension and preeclampsia to those born to mothers with normal blood pressure by gestational age. The differences in mean birth weight between preeclampsia and the normotensive group ranged between -547.5 g and +239.5 g at each gestational age category from 32 weeks to 42 weeks. The birth weights were statistically significantly lower in mothers with preeclampsia delivering 37 weeks or less, with an average difference of -352.0 g. However, the birth weights were not lower in mothers with preeclampsia delivering after 37 weeks, with an average difference of +49.0 g. In Alberta, 61.2% of preeclamptic patients gave birth after 37 weeks. We conclude that most babies born to mothers with preeclampsia at term have normal fetal growth. This finding does not endorse the currently held theory that reduced uteroplacental perfusion is the unique pathophysiologic process in preeclampsia.

#### History of abortion, preterm birth and the risk of preeclampsia: a population-based study

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Preeclampsia is primarily a disease of the first pregnancy as its risk is markedly decreased in pregnant women who have had a previous pregnancy. However, evidence relating previous abortion, and preterm birth to the risk of preeclampsia is scarce and conflicting. In order to examine the relationship between prior abortion, preterm birth and preeclampsia, we conducted a population-based retrospective cohort study of 140773 pregnancies delivered between 1993 and 1999 in 49 hospitals in Northern and Central Alberta of Canada. We found that in nulliparous women, there was no significant difference in the incidence of preeclampsia between women with previous abortion (2.6%) and without abortion (2.9%). The adjusted odds ratio (aOR) was 0.89 (95% confidence interval [CI] 0.78-1.01). In women without previous history of abortion and term pregnancy, there was no significant difference in the incidence of preeclampsia between women with previous preterm birth (2.7%) and nulligravid women (2.8%). The aOR was 0.71 (0.48-1.03). The incidence of preeclampsia was markedly lower in multiparous women without prior history of abortion and preterm birth (0.9%) than in nulligravid pregnancies (2.9%). The aOR was 0.29 (0.26-0.33). The adjusted ORs of preeclampsia for women with 1, 2, 3, and 4 or more previous pregnancies were 0.32 (0.28-0.36), 0.27 (0.22-0.34), 0.22 (0.15-0.33), and 0.21 (0.12-0.35), respectively. We conclude that only a history of term pregnancy (>37 weeks) conveys a substantial 'protection' against preeclampsia in the subsequent pregnancy.

#### Health and risk behavior of children from immigrant families in the US

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A significant proportion of US children come from immigrant families and may face a host of adverse school and health factors. This study used data from 15 686 11- to 16-year-old-children who participated in the 1997–98 WHO Health Behavior in School-Aged Children Survey to compare the health and risk behavior of US children from immigrant and non-immigrant families. Language spoken at home was used as a proxy to identify family's immigrant status. Immigrant families were defined as families that speak only or mostly another language or families that speak English and another language equally (83%).

Families that speak English only were considered non-immigrants (17%). Weighted data analyses were conducted using SUDAAN. 3413 (weighted N = 3219606) children in the survey come from immigrant families, 72% of whom were born outside the US, representing 5.9% of non-Hispanic white, 7.7% of non-Hispanic black, 69.5% of Hispanic, 67.7% of Asian children nationwide. Compared with children from non-immigrant families, children from immigrant families are significantly less likely to consider themselves healthy, to always wear a seat belt and bicycle helmet, to exercise, to see a doctor or nurse for any injury, to have their own bedroom, to have a father who is employed, and to have a close friend. They are more likely to belong to a minority race and watch TV 4 h a day or more. On the other hand, they are not significantly different from children of non-immigrant families in smoking or marijuana use and bullying or fighting behaviors. More research should be targeted to elucidate the complex health and school needs of immigrant children.