

# Gestational Age Tied to Subsequent Preterm Births

*Preterm birth risk in second pregnancy inversely related to gestational age at birth in first preterm pregnancy.*

BY KAREN RICHARDSON  
Contributing Writer

QUEBEC CITY — Women who've had a prior preterm birth are at increased risk for a subsequent preterm birth and associated neonatal morbidity and mortality, and this risk is inversely related to the gestational age at which their first spontaneous preterm birth occurred.

That finding emerged from a population-based cohort study of more than 25,000 women that was presented at the annual meeting of the Society of Obstetricians and Gynaecologists of Canada.

Women with a previous preterm birth, especially if it's earlier than 34 weeks, are at high risk and should be monitored carefully, said Erica Frecker, M.D., a resident in obstetrics and gynecology at Dalhousie University in Halifax, N.S., working under B. Anthony Armson, M.D.

The study offers useful information for obstetricians who give preconceptional counseling to women with previous preterm births, who are often worried about the outcome of their next pregnancy, said Dr. Frecker, the study's lead author.

Using the Nova Scotia Atlee Perinatal Database, researchers identified 25,525 women who had their first and second de-

liveries in 1988-2001. All of the women had spontaneous births; stillbirths and major fetal anomalies in the first pregnancy were excluded.

The women were categorized into four groups based on their babies' gestational ages at first delivery. The risks of preterm birth and serious neonatal morbidity or mortality in the subsequent pregnancy were calculated using multivariate analysis.

The incidence of preterm birth earlier than 37 weeks, earlier than 34 weeks, and earlier than 28 weeks was 4.66%, 1.25%, and 0.3%, respectively, in the first pregnancy, followed by an incidence of 3.66%, 0.94%, and 0.24%, respectively, in the second pregnancy.

The relative risk of having a preterm birth in the second pregnancy was inversely related to the gestational age at birth in the first pregnancy, except in the youngest gestational age category. (See chart.)

The numbers were adjusted for multiple gestation and uterine anomaly by multivariate regression.

The proportions of neonatal morbidity/mortality in the second pregnancy increased as the gestational age category decreased. The proportions increased from 1.21% for gestational ages greater than 37

weeks to 8.18% for gestational ages of less than 28 weeks. Serious neonatal morbidity cases included necrotizing enterocolitis, severe respiratory distress syndrome, bronchopulmonary dysplasia, sepsis, pneumonia, and meningitis.

Commenting on the study, David Young, M.D., past president of the Society of Obstetricians and Gynaecologists of Canada, noted that the results from the provincial perinatal database may be applicable to the general population, as they represent every birth in Nova Scotia for 1988-2001. "Researchers or clinicians in the field, particularly of preterm birth, would not be surprised by these results, but it adds substantially to the information that already is available and what might have been our best guess," said Dr. Young, now head of the department of obstetrics and gynecology at Dalhousie University's IWK Health Centre in Halifax.

Although "we don't have a proven, ef-

fective method of intervention," Dr. Young said, the study may shed light on the controversy surrounding intramuscular progesterone, which was the subject of several studies, including a randomized, controlled trial (N. Engl. J. Med 2003;348:2379-85). Since then, a more recent review has been published on the prevention of preterm delivery using the same medication (Obstet. Gynecol. 2005;105:1128-35).

"It [progesterone] may be the closest thing that might be effective," Dr. Young said.

The study results also provide evidence that women who have a prior preterm birth—particularly those who delivered earlier than 34 weeks—should be monitored more closely, noted Dr. Young. These patients may be considered for investigations such as cervical length surveillance through transvaginal ultrasound, for the treatment of prophylactic steroids for lung maturity, and for modification of activity. ■

## How Likely Is a Second Preterm Birth?

Gestational Age at First Birth	Relative Risk of Second Preterm Birth
≥37 weeks	1.00
34-36 weeks	4.47
28-33 weeks	9.22
<28 weeks	7.09

Source: Dr. Frecker

KEVIN FOLEY, RESEARCH

## Large Study Questions Possible Steroid/Orofacial Cleft Link

BY SHARON WORCESTER  
Tallahassee Bureau

ST. PETE BEACH, FLA. — The use of oral steroids for asthma during pregnancy has long been discussed as a possible cause of orofacial clefts in newborns, but findings from a large cohort study suggest this is not the case.

In nearly 82,000 mother/infant pairs, not a single infant with an orofacial cleft was born to any of the more than 400 women who received at least one oral steroid prescription in the 90 days before pregnancy or during early pregnancy, Janet R. Hardy, Ph.D., reported at the annual meeting of the Teratology Society.

The findings could put an end to long-held beliefs—based on findings in laboratory animals decades ago—that a link exists between the medication and an increased risk for such defects.

About 6% of mothers in the retrospective population-based cohort study were asthmatic, and nearly 2% had other respiratory conditions. A total of 130 babies included in the study were born with orofacial cleft; only 6 of these were born to asthmatic mothers, and 3 others were born to women with other respiratory conditions. None of the nine mothers had received a prescription for an oral steroid during pregnancy, said Dr. Hardy, of the University of Massachusetts, Worcester.

The relative risk of cleft overall in this

study was 1.30; the relative risk in babies born to women who received a prescription for any type of steroid medication was 1.26.

Dr. Hardy noted that the study, based on data in automated medical records from 1991 to 1999, is limited by its basis on prescribed medications. Medications prescribed do not necessarily equate to medications taken, she said, noting that she also was unable to study asthma severity, maternal smoking, family history, and racial and ethnic background.

Adjustment for other possible confounders, including other medications used, did not affect the results, however, she said.

Asthma complicates 3.7%-8.4% of pregnancies, and these findings suggest that any steroid use is associated with only a slightly increased risk of orofacial clefts.

Given the small overall risk with any steroid use and the apparent absence of risk with oral steroids, it is of concern that the data show a decline in the prescribing of oral steroids for the treatment of asthma in the first trimester, Dr. Hardy said.

In the prepregnancy period, 318 mothers (including 203 who were asthmatic) received at least one oral steroid prescription. In early pregnancy, however, only 149 (including 89 who were asthmatic) received at least one oral steroid prescription.

The risks associated with uncontrolled asthma are likely to be worse for the fetus than the risks of asthma medications, she concluded. ■

## High Fetal CO Exposure May Up Gastroschisis Risk

BY SHARON WORCESTER  
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ST. PETE BEACH, FLA. — Young pregnant women who smoke cigarettes or marijuana or who are malnourished have a significantly increased risk of having an infant with gastroschisis, a case-control study suggests.

Those who have both risk factors have an even greater risk of having an infant with this severe birth defect, Phung Kim Lam, Ph.D., reported at the annual meeting of the Teratology Society.

Dr. Lam studied 55 infants with gastroschisis and 94 age-matched controls. Maternal information was based on interviews and food-frequency questionnaires.

Mothers were said to have high carbon monoxide (CO) exposure if they smoked at least one pack of cigarettes daily near the time of conception or if they smoked marijuana habitually around that time, said Dr. Lam of the University of California, San Diego.

Malnutrition was characterized by

protein intake of less than 72 g/day, zinc intake of less than 10 mg/day, and maternal body mass index of less than 22 kg/m<sup>2</sup>; these three factors were highly correlated (low zinc with low protein, and low protein with BMI).

**Young mothers without low BMI but with high CO exposure were more likely than controls to have a baby with gastroschisis.**

They are also correlated with numerous other markers of nutritional status, such as intake of certain other vitamins and minerals.

On multiple conditional logistic regression, gastroschisis was associated with high CO exposure (odds ratio 2.64) and low animal protein intake (OR 2.45).

Young mothers without low BMI but with high CO exposure were more likely than controls to have a baby with gastroschisis (odds ratio 16.81), as were those with low BMI and no CO exposure (OR 19.69). But the finding was much more marked in those with low BMI and high CO exposure, compared with controls (OR 26.49), she said.

The findings support those of an animal model in which exposure to high levels of carbon monoxide and low protein and zinc intake in pregnant mice led to this birth defect. ■