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Treatment of maternal hyperthyroidism can be problematic in some pregnancies ►

In an estimated 0.2% of pregnancies, women have thyrotoxicosis that requires therapy. The most commonly used antithyroid drugs cross the placenta, and reports of possible teratogenic effects of methimazole (MZ) and carbimazole (CZ) have been appearing since the 1970s. In this case report and literature review, the authors ask whether a rare phenotype is associated with prenatal CZ exposure.

The authors report the cases of two children with in utero exposure to CZ and remarkably similar, distinctive clinical presentations: short, upslanting palpebral features, small nose with broad nasal bridge, and broad forehead. Aplasia cutis of the scalp; GI tract anomalies (including imperforate anus, esophageal atresia, omphalocele, and bilateral choanal atresia); hypoplastic nipples and breasts; a variety of congenital heart defects; developmental delay; and hearing loss have also been reported after in utero exposure to MZ and CZ. The authors note the importance of controlling maternal thyroid function before and during pregnancy to prevent fetal loss, low birth weight, preterm labor, hydrops, fetal goiter, and newborn craniosynostosis. They also point out that the frequency of CZ/MZ-associated complications is unknown and that infant outcomes in most such pregnancies are good.

Comment ► As with many other drugs, a genetic susceptibility must be present in the mother, the infant, or both for the teratogenic effects to occur. Pediatricians should be aware of the features of methimazole and carbimazole complications and ask about maternal thyroid status.

Judith G. Hall, OC, MD

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▲ **Foulds N et al.** Carbimazole embryopathy: an emerging phenotype. *Am J Med Genet* 2005;132A:130-5.

Meningococcal vaccine: a step in the right direction ►

Meningococcal polysaccharide vaccine has not been recommended for the general population because of its relatively poor immunogenicity and short-lived protection. A new protein-conjugated vaccine (Menactra) developed for use against the same four serogroups (A, C, Y, and W-135) was approved for use in adolescents in January 2005. These investigators compared the safety and effectiveness of the polysaccharide and the conjugated meningococcal vaccines in a group of 1398 children (age range, 2-10 years).

Seroconversion rates of all four serogroups were better with the conjugate vaccine than with the polysaccharide vaccine (group A, 98.6% vs. 94.7%; group C, 87.9% vs. 80.1%; group Y, 86.2% vs. 75.0%; and group W-135, 96.0% vs. 89.6%). Mean geometric titers were also significantly higher in the group given the conjugate vaccine. The only adverse effects were mild, local reactions, and they occurred similarly in both groups.

Comment ► These results demonstrate that the protein-conjugated meningococcal vaccine has great promise in children. Until more data are available, physicians should implement the new Advisory Committee on Immunization Practices recommendations to immunize all 11- and 12-year-olds, students entering high school,

and college freshmen who will be living in dormitories. It is also essential to remember that no meningococcal vaccine protects against serogroup B, which still accounts for a considerable number of cases.

Peggy Sue Weintrub, MD

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▲ **Pichichero M et al.** Comparative trial of the safety and immunogenicity of quadrivalent (A, C, Y, W-135) meningococcal polysaccharide-diphtheria conjugate vaccine versus quadrivalent polysaccharide vaccine in two- to ten-year-old children. *Pediatr Infect Dis J* 2005;24:57-62.

The impact of varicella vaccine ►

The introduction of the universal childhood varicella vaccination program in 1995 was controversial because many clinicians and parents did not believe in the need to immunize for a "benign" disease. CDC investigators have tallied the annual deaths, from 1990 through 2001, in which varicella was the underlying or contributing cause.

Deaths attributable to varicella declined significantly after introduction of the vaccine: from 105 deaths per year in the period 1990-1994 to 48 in 1999, 40 in 2000, and 26 in 2001. Deaths in which varicella was a contributing cause also declined, from 39.6 per year in the period 1990-1994 to 26.7 per year in the period 1999-2001. The average age-adjusted mortality rate for varicella as an underlying or contributing cause declined by 59%, from 0.56/1,000,000 in 1990-1994 to 0.23/1,000,000 in 1999-2001. Although death rates declined in all age groups below 50 years, the greatest decline (92%) was among children aged 1 to 4 years. Mortality rates were similar in all racial and ethnic groups and regardless of birthplace.

Comment ► The addition of varicella vaccine to the routine immunization schedule has been worthwhile. Aside from reduced mortality rates, the rates of other adverse effects related to varicella infection have also declined (e.g., missed school or work, hospitalization for complications). Whether waning immunity will necessitate repeat vaccination remains an important question.

Howard Bauchner, MD

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▲ **Nguyen HQ et al.** Decline in mortality due to varicella after implementation of varicella vaccination in the United States. *N Engl J Med* 2005;352:450-8.

Bladder ultrasound before urethral catheterization ►

Catheterized specimens are the gold standard for urine culture in infants (age, 0-24 months). The procedure is relatively uncomfortable and invasive and, if the bladder is empty, produces an inadequate amount of urine and must be repeated. Researchers based in a medical center emergency department assessed the value of precatheterization bedside ultrasound to predict adequate urine volume in the bladder.

In the observation phase (a prospective, unrandomized control study in 136 children younger than 24 months), precatheterization US predicted successful collection (>2 mL of urine) in 72% of patients. Success was greater in boys than in girls (77% vs. 65%). In the intervention phase, in a second group of 112 infants, sufficient urine was identified by the first US in 76% of patients, and 98% of

them had successful catheterization. A repeat US was done 90 minutes later in those whose initial scan showed inadequate urine volume, and 93% of these patients had successful catheterization on the first attempt. The overall success rate with this approach was 96%, a significant improvement over rates observed in the observation phase ($P < 0.001$). The rates in boys and girls were 98% and 93%, respectively. Limitations of the study include lack of blinding and randomizing, and an assumption of universal physician proficiency.

Comment ► Bladder catheterization can be significantly improved by prior documentation of urine in the bladder. This strategy requires newly available portable ultrasound equipment and appropriate training of staff, but it seems worthwhile to make the effort to improve the effectiveness of this valuable procedure.

Harlan R. Gephart, MD

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▲ **Chen L et al.** Utility of bedside bladder ultrasound before urethral catheterization in young children. *Pediatrics* 2005;115:108–11.

Statins and low cholesterol may be bad news for human embryos and fetuses ►

The FDA currently classifies statins as pregnancy category X (contraindicated) drugs, based on animal studies and the importance of cholesterol biosynthesis in fetal development. In this report, NIH scientists analyzed patterns suggestive of teratogenic effects in all currently available case reports of statin exposure during gestation.

Among 214 ascertained exposures, 70 remained after excluding cases that involved selective or spontaneous first-trimester abortion, known maternal or fetal complications, or insufficient information. Adverse outcomes were reported in 31 of the 70 cases: 22 had structural defects, including severe midline central nervous system defects, limb deficiencies, and VATER or VACTERL association (>3 associated defects of the vertebra, anus, cardia, trachea, esophagus, kidneys, or limbs); 4 had intrauterine growth restriction; and 5 died in utero. All abnormalities were associated with exposure to lipophilic statins—cerivastatin, lovastatin, simvastatin, or atorvastatin—which can reach the embryo and fetus and can be expected to down-regulate the biosynthesis of cholesterol. No abnormalities were associated with exposure to pravastatin, a nonlipophilic statin.

Comment ► Given the results of this uncontrolled study, the possibility of increased statin use among women of childbearing age is worrisome, as is the recent trend in the U.K. to sell statins over the counter. When a congenital anomaly is present, pediatricians should ask about the use of cholesterol-lowering drugs during pregnancy. As the authors make clear, the highest priority should be given to epidemiologic, controlled studies of the teratogenic potential of these drugs.

Judith G. Hall, OC, MD

Published in *Journal Watch Pediatrics and Adolescent Medicine* March 14, 2005

▲ **Edison RJ, Muenke M.** Mechanistic and epidemiologic considerations in the evaluation of adverse birth outcomes following gestational exposure to statins. *Am J Med Genet* 2004;131A:287–98.