



Disclaimer: This newsletter, provided by ITIS, is funded by a grant from the Illinois Department of Public Health and supported by Northwestern Memorial Hospital and Northwestern University Medical School. It is for educational purposes only and is meant to summarize the information available at the time of its creation. It should be construed neither as medical advice nor opinion on any specific clinical situation. For more information on a specific clinical situation, or updated information, please consult your health care provider.

Thyroid Disease and Pregnancy

Vol 5#4, April 1997

Eugene Pergament, MD, PhD; Amy Stein Schechtman, MS; Jaime Follmer

It is currently estimated that between 5 and 10% of all women have thyroid disease. The effects of thyrotoxicosis on pregnancy are variable and dependent upon metabolic maintenance; untreated conditions may result in low birth weight, congenital malformations, spontaneous abortion or neonatal death.

Since thyroid disease must be closely monitored and treated to maintain metabolic stability, this issue of RISK||NEWSLETTER will address the effects of thyroid disease and its treatment on pregnancy.

HYPOTHYROIDISM

Overt hypothyroidism is frequently associated with infertility. This is because in hypothyroidism, as in an autoimmune disorder, white blood cells are recruited to attack ovarian proteins; the result is ovulatory failure. For this reason, maternal hypothyroidism usually does not appear in conjunction with pregnancy.

The most common inherited cause of thyroiditis is Hashimoto disease; this form of hypothyroidism accounts for 8% of the women with thyroid disease (Burrow, 1992). In this chronic, inflammatory disorder, the thyroid is attacked by abnormal antibodies and white blood cells. The damaged gland produces progressively less thyroid hormone while concurrently, the pituitary gland secretes thyroid-stimulating hormone. Stimulated to increase activity, the thyroid may enlarge, producing a goiter.

Complications may arise following alterations in metabolic activity, therefore pregnant hypothyroid patients have a higher incidence of adverse pregnancy outcome when compared with the general population. Spontaneous abortion, stillbirths and low birth weight are the most common effects (Nuwayhid, Essentials of Ob/Gyn, 1986). To avoid both maternal and fetal complications, many pregnant hypothyroid patients follow strict thyroid hormone replacement therapy.

The incidence of congenital hypothyroidism is approximately 1 in 4,000 births. The causative factors include thyroid dysgenesis, inborn errors of thyroid function and drug induced endemic hypothyroidism. Thyroid hormone deficiency during early fetal development may lead to developmental and mental retardation. Congenital heart defects, more specifically septal defects and pulmonary stenosis, were increased to 4.3% (from 2.5% in controls) in infants born with congenital hypothyroidism (Balestrazzi et al., 1994). In addition, newborns who are not able to manufacture adequate thyroid hormone require immediate attention to prevent vision impairment, facial deformities and muscle weakness that may arise as the child matures (Nuwayhid, Essentials of Ob/Gyn, 1986).

The severity of these symptoms is dependent on the timing and degree of thyroid hormone deprivation. If the disease can be diagnosed and treated early, the effects of such deprivation may be minimal.

HYPERTHYROIDISM

Hyperthyroidism during pregnancy is frequently associated with Graves disease. Persons affected with Graves disease inappropriately create antibodies that attach themselves to the thyroid, i.e., Graves disease is an autoimmune disorder. These antibodies stimulate the thyroid to produce abnormally high levels of thyroid hormone, lending the thyroid feed-back mechanisms useless (Suarez, 1997).

Subacute thyroiditis is a second cause of hyperthyroidism during pregnancy. Approximately half of all patients with subacute thyroiditis develop hyperthyroidism. Evidence suggests that this is a transient condition induced by viral infection; most patients experience a throat infection prior to thyroiditis (Thyroid Foundation of Canada, 1992).

Maternal complications associated with hyperthyroidism are not unusual during pregnancy. The resulting consequences can include gestation-induced hypertension, congestive heart failure, toxemia and proximal muscle weakness (Kohlmeier, 1995). Hydatidiform moles should also be considered when a patient develops hypermetabolic symptoms for the first time in pregnancy.

The most immediate threat for a pregnant patient with thyrotoxicosis is the onset of a "thyroid storm". Precipitating factors include infection, labor, cesarean section, or noncompliance with prescribed medication. The storm's incipience is marked by hyperthermia, tachycardia, perspiration, and severe dehydration. Despite innovative medical intervention, maternal mortality exceeds 25% (Nuwayhid, Essentials of Ob/Gyn, 1986).

Approximately 1% of pregnant women with Graves disease will give birth to a child with thyrotoxicosis. While this is a transient condition, it poses a substantial threat; a neonatal mortality rate of 15% is associated with placental transfer of thyroid stimulating immunoglobulins (Nuwayhid, Essentials of Ob/Gyn, 1986). However, the risk of neonatal thyrotoxicosis is not confined to mothers with untreated Graves disease. Thyroid antibodies from euthyroid mothers are able to cross the placenta causing fetal hyperthyroidism in 2-12% of infants born to mothers with Graves disease. Tachycardia, congestive heart failure, intrauterine growth retardation and preterm delivery are the most common consequences (Treadwell et al., 1996).

TREATMENT

THYROXINE

Thyroxine (synthroid) is the most common thyroid hormone replacement therapy for hypothyroidism. Due to hypothyroidism's association with adverse pregnancy outcome, available case reports do not recommend that women who require thyroxine be denied this hormone treatment during pregnancy (Lowell et al., 1988).

The Collaborative Perinatal Project followed 537 first trimester exposures to thyroxine and found no increased frequency of minor or major congenital malformations. The remainder of the study observed 1,605 children exposed through the duration of their mother's pregnancy which revealed no increase in the frequency of congenital malformations (Heinonen et al., 1977).

Thyroxine has also been utilized in utero to enhance lung maturity in the fetus. Barkai et al. studied the effects of such treatment on 18 children ages 5 to 6 years. They found no long-term effects on psychomotor development from intrauterine thyroxine exposure during the last trimester (Barkai et al., 1988).

Thyroxine is secreted in small amounts into breast milk, therefore it has not been contraindicated during feeding. Because it is present in such small quantities, it does not compensate thyroid hormone quantities in newborns with congenital hypothyroidism (Abassi et al., 1980).

RADIOIODINE

Radioiodine is an effective treatment for thyroid carcinoma and hyperthyroidism. Studies have suggested that the human oocyte is resistant to radioiodine at levels up to 400 rads. Gonadal exposure to radioiodine, however, sometimes exceeds this threshold. In studies of fertility and abnormal births among 105 women who received I-131 for thyroid ablation, the only abnormal births were detected in pregnancies that began less than 1 year after radioiodine treatment (Smith, 1994; Balan, 1994; Casara, 1994). This has led to the recommendation that pregnancy be avoided for at least 12 months after radioiodine therapy.

A study by Schlumberger (1996) reported on abnormal births of conceptions that occurred less than a year subsequent to I-131 exposure. Normal fertility was observed in 2,113 pregnancies following I-131 treatment, with a low incidence of congenital malformations that was not significantly different before or after treatment. Fifty-seven children born with congenital malformations had maternal exposures more than one year prior to conception, compared with 61 children born whose mothers conceived less than one year following treatment. While there was no apparent pattern of anomalies, 6 cases of malignancies were discovered at sites other than the thyroid in exposed children; 4 of these were leukemias with one case occurring in a mother who was exposed less than one year prior to conception.

The incidence of miscarriage was slightly elevated, however, in mothers exposed to I-131. Eleven percent of miscarriages occurred before treatment and 20% were reported after radioiodine exposure. Miscarriages were more frequent in the 10 women who underwent treatment less than one year prior to conception (Schlumberger, 1996).

While there have been several cases of normal offspring born to women who were inadvertently exposed to I-131 early in pregnancy, administering radioiodine after the tenth week of conception still has the potential to cause damage to the fetal thyroid gland (Russell et al., 1957). The eleventh week post-conception is marked by the thyroid's ability to concentrate iodine, thus rendering it susceptible to I-131 treatment.

Breast feeding is also not recommended if radioiodine is administered during lactation. The mammary gland has a strong affinity for iodine and it is suggested that at least 52 days are necessary to reduce levels of iodine in the mammary gland to safe levels for a newborn (Robinson et al., 1994).

PROPYLTIOURACIL

PTU, considered by many to be the antithyroid medication of choice during pregnancy, has the ability to cross the placenta. In rare situations PTU may be hepatotoxic in the infant. Because placental transfer can suppress fetal thyroid function, fetal thyroid hyperplasia and goiter are sometimes discovered on ultrasonography, as the fetus attempts to compensate for hypothyroidism (Solomon et al., 1981). Since treatment of Graves disease patients with PTU can result in congenital hypo/hyperthyroidism, neonatal thyroid function should be screened at birth. The occurrence of major malformations in fetuses exposed to PTU in utero was not increased above the general population. Moreover, the frequency of malformations was not significantly increased among the children of 65 women with Graves disease who were treated with PTU during pregnancy when compared to the children of untreated Graves patients (Momotani et al., 1991).

Two long-term studies of children whose mothers took PTU during pregnancy indicated no significant differences in growth, cognitive or motor development. Messer et al. (1990) compared 17 children whose mothers took PTU to 25 children whose mothers were euthyroid and had no treatment. Birth weight was significantly lower in the former group, but individual body weights were normal for gestational age. However, the body weight differences disappeared following further development. A subsequent study compared offspring ranging from 3 to 25 years whose mothers took PTU during

pregnancy with children whose mothers did not and found that the two groups did not differ significantly in psychomotor evaluations. Another study by Burrow et al. (1978) compared 28 offspring ages 2 to 28 years with those unexposed; 23 of the exposed group had third trimester exposure. No differences were observed between these two groups on performance on intellectual tests.

PTU is secreted into breast milk in small amounts. The World Health Organization has stated that the use of this drug in conjunction with breast feeding is safe for the infant. Steps should be taken to monitor the infant's thyroid function.

THYROID DISEASE & GENETICS

In the 1970's prenatal diagnosis was routinely offered to women with thyroid conditions. In a 1966 study, Fialkow et al. reported that the frequency of thyroid autoantibodies was significantly higher in mothers of patients who have Down syndrome compared to controls. Even more prominent were the differences among younger mothers of patients with Down syndrome (Milunsky, Genetic Disorders and the Fetus, 1988). In spite of these past reports, maternal autoimmune disorders are not associated with Down syndrome.

SUMMARY

Thyroid disease is relatively common among women of all ages. This condition can be effectively treated and does not appear to directly cause significant health problems. Difficulties may arise, however, for pregnant mothers with thyroid disease. Maintenance of thyroid control during pregnancy is crucial to avoid complications or adverse pregnancy outcome. Pregnant mothers may have to weigh the risks and benefits of thyroid treatment, compared to those associated with not maintaining thyroid control. Many studies have indicated that there is no increased risk of birth defects for infants born to mothers treated for thyroid disease; thyroxine and PTU appear to pose no significant risks to the developing fetus. The consequences of non-treated thyroid disease may, in fact, be more threatening to both mother and fetus.