AACE Position Statement

SUBCLINICAL HYPOTHYROIDISM DURING PREGNANCY: POSITION STATEMENT FROM THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS

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THYROID HORMONES AND FETAL DEVELOPMENT

The importance of thyroid hormones for normal fetal development is well established. Through animal experiments (1,2) and clinical studies (3,4), thyroid hormones have been clearly found to be crucial in brain development, maturation, and normal function. The fetal thyroid begins to produce thyroid hormones at about 10 to 12 weeks of gestation.

During the first trimester, thyroid hormones are supplied exclusively by the mother, whereas during and after the second trimester, thyroid hormones are supplied by both the mother and the fetus (although probably primarily by the mother). Maternal thyroxine (T_4) is important for fetal neural development throughout pregnancy but particularly during the first trimester, when it is known to cross the placenta in substantial amounts (5).

Maternal thyroid dysfunction during pregnancy can result in impaired psychoneurologic development of the fetus. Maternal hypothyroidism has been associated with mental retardation in the living euthyroid offspring as well as with increased fetal and neonatal losses (6). Pharoah and associates (3) showed that the intelligence of the euthyroid offspring of women with endemic hypothyroidism correlated with maternal thyroid hormone levels during pregnancy. When the mother has hypothyroidism, fetal brain development could be impaired by lack of sufficient T_4 before fetal thyroid function begins or even after the onset of fetal thyroid function if maternal antibodies such as thyrotropin-binding inhibitory immunoglobulins reduce fetal thyroid hormone production (7). In 1995, Pop and colleagues (8) reported that children of pregnant women with normal thyroid function but increased thyroid peroxidase antibodies (TPO-Ab) were at risk for impaired psychomotor development. Because such impairment was not associated with actual thyroid dysfunction, it is unclear whether the autoimmunity itself is responsible or whether "TPO-Ab may merely be the surrogate marker for T_4 levels in the mother" (5). In a more recent study by the Dutch group (9), they reported that low maternal free T_4 concentrations in apparently healthy women during early gestation are associated with a significantly increased risk of impaired neurodevelopment in the infant. These observations suggest that mild (subclinical) hypothyroidism early during pregnancy may adversely affect fetal psychoneurologic development.

In a recent report, Haddow and associates (10) provide additional evidence that subclinical hypothyroidism early during pregnancy may be harmful to fetal development. In a retrospective study, they measured thyrotropin concentrations in stored serum samples collected between 1987 and 1990 from 25,216 pregnant women during their second trimester. From these samples, they identified 62 women who had mild increases in thyrotropin levels during pregnancy. None of the children of these women had hypothyroidism when tested at birth. The children of these women were then studied at 7 to 9 years of age and compared with children of 124 matched control women. Both groups were subjected to 15 tests relating to intelligence, attention, language, reading ability, school performance, and visual-motor performance. Those children whose mothers had hypothyroidism during pregnancy performed less well on all tests. The full-scale IQ scores in these children averaged 7 points lower than those of the 124 matched control children; 19% of these children had IQ scores of 85 or less in comparison with 5% of the children with normal maternal thyroid function. Many of the women with high thyrotropin levels also had elevated TPO-Ab; 11 years after the pregnancy, 64% of these women in comparison with only 4% of the matched control women had clinical hypothyroidism.

The report by Haddow and colleagues (10) confirms earlier findings that mild maternal hypothyroidism can adversely affect fetal brain development. On the basis of their findings, these authors suggest that all pregnant women should be screened for hypothyroidism by serum thyrotropin determination. The IQ deficit in the children in this study was small, and other factors besides mild maternal hypothyroidism could have been causally related. Nonetheless, the clinical relevance of this important study directs attention to the role of maternal thyroid hormone production and function on brain development during early pregnancy in an iodine-sufficient area.

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RECOMMENDED GUIDELINES

The American Association of Clinical Endocrinologists (AACE) believes that, until further data are available, the following medical guidelines should be considered by those physicians involved in the care of pregnant women:

- Routine serum thyrotropin testing early during pregnancy is reasonable but should be left to the judgment of the physician, in consultation with the patient.
- In all pregnant women with a goiter, high antithyroid antibody titer, family history of thyroid disease, any history of other autoimmune endocrine disease, or symptoms suggestive of hypothyroidism, serum thyrotropin testing should be performed.
- In pregnant women found to have an increased serum thyrotropin level, even if mild, levothyroxine therapy should be promptly initiated if repeated thyrotropin determinations remain elevated.
- Inasmuch as the levothyroxine requirement is increased during pregnancy (11,12), all women who are already taking levothyroxine before pregnancy should undergo serum thyrotropin testing; if the thyrotropin level is elevated, the levothyroxine dose should be appropriately increased.
- Pregnant women who have high TPO-Ab titers but normal serum thyrotropin levels should undergo careful postpartum and long-term follow-up because of the high probability of subsequent clinical hypothyroidism.
- Serum thyrotropin testing should be done in all women considering pregnancy so that hypothyroidism can be diagnosed early and treated before pregnancy.

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