THYROID
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Consensus Statement #2

American Thyroid Association Statement on Early Maternal Thyroidal Insufficiency: Recognition, Clinical Management and Research Directions

FOR MORE THAN 100 years, it has been clear that adequate maternal iodine nutrition, and more recently, adequate maternal thyroid hormone is necessary during and after pregnancy to ensure the health of the mother and her offspring. Adequate maternal iodine nutrition must be maintained during pregnancy to meet the increased demand for thyroid hormone production that occurs with pregnancy. Maternal iodine supplies in the United States and in most of the developed world are now sufficient to prevent the occurrence of cretinism and severe mental retardation from iodine deficiency. However, there are still additional adverse outcomes for maternal health, maintenance of pregnancy, and child development that may occur as a result of overt maternal hypothyroidism, as well as subclinical hypothyroidism (normal serum thyroxine concentration and elevated serum thyrotropin [TSH] concentration), maternal hypothyroxinemia (depressed serum free thyroxine concentration), and the presence of thyroid autoantibodies.

Key research findings include:

- Pregnant mothers with overt or subclinical hypothyroidism are at an increased risk for premature delivery.
- Pregnant mothers with detectable thyroid autoantibodies and normal thyroid function are at an increased risk for miscarriage and for postpartum thyroid disease including thyroiditis, hyperthyroidism (Graves' disease), and also hypothyroidism.
- The offspring of mothers with thyroid hormone deficiency or thyroid stimulating hormone elevation during pregnancy may be at risk of mild impairment in their intellectual function and motor skills.
- Pregnant women being treated with thyroid hormone replacement often require a 30%–50% increase in their thyroid hormone dose.

Clarification of the magnitude of these problems is urgently needed, as is the development of programs for their management.

Women with Known Thyroid Disease or Known Risk for Thyroid Disease

It is clear that women with a history of thyroid disease, thyroid autoimmunity, or a family history of thyroid disease should have their thyroid health evaluated before planning pregnancy and again shortly after becoming pregnant. This is also true for women with type 1 diabetes mellitus or with non-thyroid autoimmune diseases.

Pregnant women with overt hypothyroidism should be treated for their own health as well as for the health of their children. The majority of women who are being treated with thyroid hormone replacement require a 30%–50% increase in their thyroid hormone dose when pregnant. A significant number of women with diagnosed hypothyroidism may be undertreated for part or much of their pregnancy. Therefore, the adequacy of their thyroid hormone levels should be assessed regularly during pregnancy. Women with subclinical hypothyroidism should also have their thyroid status monitored throughout pregnancy. Fetal development that is reliant on the presence of thyroid hormone appears dependent on adequate maternal thyroxine (T_4) levels, and not circulating triiodothyronine (T_3) levels. Therefore, levothyroxine (LT_4) preparations are the preferred method for thyroid hormone replacement in pregnant women or those women contemplating pregnancy.

It is currently suspected that there are risks to the fetus and possibly to the mother from untreated subclinical hypothyroidism or from isolated hypothyroxinemia (low serum free thyroxine level and normal serum TSH). Clinical practitioners from a number of medical specialties care for women before and during pregnancy and have had different approaches to the treatment of subclinical hypothyroidism. Research programs should be developed to assess the magnitude of these conditions and consequences related to their treatment or nontreatment. Pilot programs should be developed to assess the efficacy, cost, and benefits of screening programs before they are instituted.

Once the magnitude of the above listed issues has been determined, consideration should be given to performing randomized placebo-controlled clinical trials in order to examine the risks and benefits of treating maternal subclinical hypothyroidism and possibly maternal hypothyroxinemia. As to ethical concerns, these studies will need to be very carefully planned, and agreement reached on which patient populations, based on clinical and laboratory criteria, are most appropriate for inclusion in such investigations. These studies should consider pregnancy end points in addition to neurodevelopmental outcomes in offspring. A recent evidence-based medicine study recommended T_4 treatment for pregnant women with subclinical thyroid disease, when identified based on symptoms or risk factors. Studies should be undertaken to determine the role of iodine status and thy-

roidal antibody status as risk factors for maternal hypothyroidism and for maternal hypothyroxinemia.

Iodine Nutrition

Optimal iodine nutrition is particularly important during pregnancy and lactation. It appears by and large that iodine nutrition in the United States is adequate, although new data suggest that some women of reproductive age in the United States may be at risk for slightly deficient intake. Iodine supplementation in pregnancy and during lactation is strongly encouraged. Total daily iodine intake is suggested to be at a level of 220 μg/d for pregnant women and 290 μg/d for lactating women, respectively. It is recommended that all prenatal vitamin–mineral supplements for use during pregnancy contain at least 150 μg/d iodine.

Plan for Action

A coordinated program of patient education, practice review, and research on the impact of maternal thyroid status on pregnancy and fetal and childhood development should be instituted by governmental institutions (Centers for Disease Control [CDC] and National Institute of Child Health & Human Development [NICHHD]), professional organizations (American Thyroid Association [ATA], American Association of Clinical Endocrinologists [AACE], The Endocrine Society, American College of Obstetrics and Gynecology [ACOG], and AAP) and nongovernmental organizations (March of Dimes, child health advocacy groups, etc.). Specific suggestions follow:

Proposed Research

- Conduct a prospective randomized placebo-controlled clinical trial examining the risks and benefits of treating maternal subclinical hypothyroidism and possibly maternal hypothyroxinemia.
- Determine trimester-specific normative data for thyroid function studies including: TSH, total thyroxine TT_4, and FT_4 for individuals with differing iodine status.
- Conduct a feasibility study for prospective population screening in a test population using filter paper specimen and central laboratory, as is now done with screening for congenital hypothyroidism in newborns.
- Clarification of the iodine nutrition status of pregnant women in the United States.
  - Measure iodine levels in breast milk and correlate with maternal iodine nutrition and factors such as smoking.
  - Establish surveillance and prospective studies in metropolitan areas to complement current programs and to serve as pilot programs for studying maternal nutrition in the United States.
  - Measure plasma inorganic iodide in pregnant women and correlate these data with urinary iodine levels.

Further research is necessary to address the following questions

- What is the prevalence of maternal overt hypothyroidism, maternal subclinical hypothyroidism, and maternal hypothyroxinemia? What are the fetal/maternal consequences of each (including post-pregnancy outcomes)?
- What role does iodine intake and/or thyroid antibodies during pregnancy play in subclinical hypothyroidism, hypothyroxinemia, or antibody-induced thyroid disease?
- What is the prevalence of iodine deficiency in pregnant women and other women of reproductive age in the United States?
- Do the guidelines for urinary iodine values for pregnant women need revision? What are the dietary iodine requirements for infants and should infant vitamins contain iodine?
- How do factors such as maternal iodine nutrition and smoking influence iodine content of breast milk and supplies to breast-fed infants?

Proposed Public Education Campaign Elements

- Education of women of reproductive age with known thyroid disease regarding the impact of hypothyroidism in pregnancy.
- Education and testing of high-risk individuals who wish to become pregnant.
- Education of all reproductive age women regarding the importance of taking a daily prenatal vitamin/mineral supplement enriched with iodine and folic acid preferably before pregnancy but at least immediately when known to be pregnant, even before the first prenatal visit.
- Education of clinicians caring for women of reproductive age on the issues of maternal thyroid disorders, identifying high-risk individuals, appropriate diagnosis, optimal treatment and monitoring. Determine the role of case finding for thyroid disease.
- Education through placement of recommendation in over-the-counter pregnancy test kits.
  - Congratulate the patient on her pregnancy, and advise the following:
    - Immediately start taking a prenatal vitamin daily—with iodine and folic acid.
    - Make an appointment with your physician for prenatal care.
  - Develop a method to rapidly assess maternal thyroid status in early pregnancy that could be included with a pregnancy test kit.
  - Indicate high thyroid health risk factors—if you fall into this category please see your doctor as soon as possible and request a TSH screening test.

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