AMERICAN THYROID ASSOCIATION
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## THYROID AND PREGNANCY

# Levothyroxine therapy of subclinical hypothyroidism or hypothyroxinemia in pregnancy does not affect brain function in the offspring

### BACKGROUND

Thyroid hormone is essential for normal brain development in the baby during pregnancy. Hypothyroidism in the mother during pregnancy has been associated with multiple complications of pregnancy. Overt hypothyroidism in the mother (high TSH and low $FT_4$) has been shown to cause a lower IQ and impaired brain development in their children. While it is clear that mild/subclinical hypothyroidism in the mother (high TSH, normal $FT_4$) also is associated with pregnancy complications, the effects on brain development in the baby is less clear. This is also true with hypothyroxemia in pregnancy, where the mother's $FT_4$ is low but the TSH is normal. Further, while screening mothers early in pregnancy will identify individuals with subclinical hypothyroidism and hypothyroxinemia, it is uncertain whether treatment with levothroxine would have any effect on pregnancy outcomes on the baby's brain development.

The current study was designed to examine the results of treatment for subclinical hypothyroidism or hypothyroxinemia detected in early pregnancy on the basis of IQ assessed in children at 5 years of age.

### THE FULL ARTICLE TITLE

Casey et al for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Treatment of subclinical hypothyroidism or hypothyroxinemia in pregnancy. N Engl J Med 2017;376:815-25.

### SUMMARY OF THE STUDY

The study was a randomized, placebo-controlled trial at 15 centers. All women who presented before 20 weeks of pregnancy were invited to be screened for TSH and $FT_4$. In the first year, TSH >3.0 was used as the basis for inclusion, but this was subsequently adjusted to >4.0 because only 6% of women had TSH >3.0. Hypothyroxinemia was set as $FT_4$ <0.86 ng/dl. Measurement of anti-TPO antibodies and urine iodine were performed. Women with subclinical hypothyroidism were randomly assigned to receive either 100 µg of levothroxine or a matching placebo capsule daily. Women with hypothyroxinemia were given 50 µg of levothroxine or placebo. The treated women had monthly measurements of TSH and $FT_4$. On the basis of the results of these measurements, doses were adjusted, with sham adjustments in the placebo groups. The goal of the levothroxine therapy was a TSH of 0.1 to 2.5 mU/L with maximum dose of 200 µg. For the hypothyroxinemia trial, the goal was $FT_4$ between 0.86 and 1.90 ng/dl. The primary outcome was the full-scale IQ at age 5 years.

From October 2006 to October 2009, a total of 97,228 pregnant women underwent thyroid screening; 3057 had subclinical hypothyroidism; 800 of these women were eligible and consented to participate. A total of 677 of them underwent randomization for the study. Hypothyroxinemia was diagnosed in 805 women, of whom 632 were eligible and 526 underwent randomization. In the subclinical hypothyroidism trial, randomization occurred before 17 weeks and 93% of the L-$T_4$-treated group achieved a TSH between 0.1 and 2.5 mU/L by 21 weeks. In the hypothyroxinemia trial, randomization occurred at 18 weeks, and 83% of women treated with levothyroxine achieved an FT4 between 0.86 and 1.90 ng/dl by 23 weeks.

In the subclinical hypothyroidism trial, the average IQ at 5 years was 97 in the levothyroxine treated group and 94 placebo group. In the hypothyroxinemia trial, the average IQ at 5 years was 94 in the levothyroxine treated group and 91 in the placebo group. None of these differences were significant. Further, there were no differences in adverse pregnancy events or outcomes between the levothyroxine treated and placebo groups in either trial.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that levothyroxine therapy for subclinical hypothyroidism or hypothyroxinemia diagnosed during pregnancy beginning at an average of 17 to 19 weeks of

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## THYROID AND PREGNANCY, continued

pregnancy had no effect on pregnancy outcomes or on brain development in children through 5 years of age than no treatment for these conditions. Because treatment has no effect, these data suggest that screening pregnant women for subclinical hypothyroidism or hypothyroxinemia is not helpful.

— Alan P. Farwell, MD, FACE

### ATA THYROID BROCHURE LINKS

Thyroid and Pregnancy: https://www.thyroid.org/thyroid-disease-pregnancy/

Thyroid Function Tests: https://www.thyroid.org/thyroid-function-tests/

Hypothyroidism: https://www.thyroid.org/hypothyroidism/

### ABBREVIATIONS & DEFINITIONS

Hypothyroidism: a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

Subclinical Hypothyroidism: a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

Overt Hypothyroidism: clear hypothyroidism an increased TSH and a decreased $T_4$ level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

Levothyroxine ($T_4$): the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyl™, Tyrosint™ and generic preparations.