Thyroid Function in the Neonatal Intensive Care Unit

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KEYWORDS

• Congenital hypothyroidism • Neonatal intensive care unit • Preterm infants
• Thyroid screening • Thyroid function testing • Thyroid testing artifacts

KEY POINTS

- Neonatal illness and prematurity may necessitate additional thyroid function screening to ensure early detection and treatment of hypothyroidism, and may alter the results and interpretation of thyroid function tests.
- Preterm infants are prone to transient hypothyroidism with delayed thyroid stimulating hormone (TSH) rise because of immaturity of the hypothalamic-pituitary-thyroid axis at birth.
- Transiently low total thyroxine (T4) and triiodothyronine (T3) levels are common during periods of neonatal illness in term and preterm infants.

INTRODUCTION

The neonatal intensive care unit (NICU) presents unique challenges to routine universal newborn thyroid screening for early detection and treatment of congenital hypothyroidism, and the interpretation of collected thyroid function tests (TFTs).[1] Preterm infants are born before hypothalamic-pituitary-thyroid axis maturation and are prone to hypothyroidism with delayed thyroid-stimulating hormone (TSH) rise and transient hypothyroidism.[2,3] In addition, illness affects the interpretation of TFTs of preterm and term sick infants.[4,5]

This article reviews normal fetal and neonatal hypothalamic-pituitary-thyroid axis development, indications for and timing of thyroid hormone testing in the NICU, medication artifacts and conditions that may affect thyroid test results, thyroid test interpretation in the NICU, evidence for and against providing thyroid hormone to NICU

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patients who have borderline TFT, and follow-up retesting of NICU infants with hypothyroidism, to differentiate transient from permanent hypothyroidism.

NORMAL IN UTERO AND POSTNATAL HYPOTHALAMIC-PITUITARY AXIS DEVELOPMENT

During the first trimester, the fetus must derive all of its thyroid hormone supply from the mother.[6] Maternal unbound thyroxine (free T4) levels increase in early pregnancy when placental human chorionic gonadotrophin, structurally similar to TSH, exhibits a weak TSH-like effect.[7] Free T4 remains elevated throughout pregnancy and is actively transported across the placenta via thyroid hormone transporters.[8,9] Although total thyroxine (T4) levels in the fetal compartments are 1/100th of maternal levels, the unbound and active fraction, free T4, is elevated relative to adults.[8,10] Iodine is also actively transported across the placenta.[11] Within the brain, type 2 and type 3 deiodinases locally convert T4 to T3, which is critical to embryonic neural cell development.[6,12]

The thyroid is the earliest endocrine structure to develop. The thyroid placode, an enlargement of the embryonic endoderm, is noted by embryonic day 22.[13] The developing thyroid begins to collect and store iodine by 10 to 12 weeks.[14] Thyroid follicles have developed by the time the fetal thyroid begins to secrete hormones into the circulation at approximately 16 weeks.[6,11] The parafollicular cells (C-cells), the neuroendocrine cells in the thyroid that produce calcitonin, develop separately. These cells differentiate from the ectoderm and move into the interfollicular connective tissue during thyroid gland development.[15] The hypothalamus develops in the first and second trimesters and it begins to take on an adult-like appearance between 24 and 33 weeks.[16,17]

T4 and free T4 serum concentrations continue to rise until they reach adult levels by 36-weeks' gestation.[18] Thyroxine-binding globulin, the primary carrier of bound T4 in the bloodstream, also rises during the second half of pregnancy.[19] However, serum concentrations of T3 and free T3 remain low throughout fetal development before a late surge prior to term.[18]

At birth, TSH, T3, and free T4 levels rapidly rise within the first postnatal half-hour.[18] However, this rise is attenuated in preterm infants because of hypothalamic-pituitary-thyroid axis immaturity. The degree of rise correlates inversely with gestational age and in the most extremely preterm infants, thyroid hormone levels decrease in the hours following birth.[20]

APPROPRIATE INDICATIONS FOR AND APPROPRIATE TIMING OF THYROID HORMONE TESTING

Congenital hypothyroidism is the most common disorder that is screened for on universal newborn metabolic screens. All infants hospitalized within the NICU should receive an initial thyroid screening test within several days of birth.[19,21] Usually this is done as part of government-mandated and -sponsored universal newborn metabolic screening. The test should be collected after 24-hours postnatal age, whenever possible, which reduces the false-positive rate especially in preterm NICU patients.[21,22] If government-sponsored metabolic screens must be collected before 24-hours because of blood transfusions that would interfere with screening results, it is important to always repeat a second screen after 24-hours postnatal age.

It must be remembered that infants may develop congenital hypothyroidism even if the initial screen within the first several days after birth had normal TSH and T4.