Infant With Suspected Congenital Hypothyroidism

Suggestive history and physical findings	Initial laboratory and/or radiologic work-up can include:	When to refer	Items useful for consultation	Additional information
-ABNORMAL NEWBORN SCREEN (NBS) for Thyroid function (Caution: NBS may be normal: keep high index of suspicion) **Symptoms/Signs:** -There may be no signs/symptoms -Lethargy, delayed meconium, enlarged fontanelles, poor temperature regulation, umbilical hernia, macroglossia, sallow skin, coarse facial features, abnormal/persistent hyperbilirubinemia, poor feeding **Family history:** In rare cases - family history of congenital hypothyroidism Differential Diagnosis	**Blood tests:** Repeat Thyroid function tests (STAT) with serum sample: • TSH • Free T4 (FT4) Other tests to consider after consultation with Pediatric Endocrinologist: • Thyroid Ultrasound • Technetium scan	**Urgent:** **All cases** of Congenital hypothyroidism should be considered a **medical emergency** and infants should be discussed with and referred to a Pediatric Endocrinologist immediately Emphasis is on phone contact with Pediatric Endocrinology. **Treatment should be started immediately (definitely within 2 weeks of birth) for optimal neurodevelopmental outcome.** Find a Pediatric Endocrinologist	Pertinent medical records (birth history), including pertinent maternal/OB history. History of maternal thyroid disease and/or maternal use of anti-thyroid medication (methimazole, PTU) Recent laboratory and radiologic studies (NBS results)	Additional Information Congenital Hypothyroidism: A Guide for Families References

Differential diagnosis for Congenital Hypothyroidism:

- Thyroid dysgenesis: thyroid agenesis, thyroid hemiagenesis, ectopic thyroid gland
- Thyroid dyshormonogenesis
- Iodine deficiency
- Central hypothyroidism
- Transient hypothyroidism: Maternal autoimmune thyroid disease; maternal medications

Additional Information

- Newborn screening for CH is jurisdiction-specific. Some programs use primary T4 screens with backup TSH testing, while others have primary TSH screens with T4 backup testing and some combine both into primary screening. Based on assay methodology, there is varying sensitivity and specificity.
- If NBS is obtained too early (< 24 hours of life), a **false positive** result can result due to physiological TSH surge that occurs several hours postnatally.
- Secondary/Central Hypothyroidism due to hypopituitarism can lead to falsely normal results in programs with primary TSH screening. Index of suspicion is key to making diagnosis. Signs suspicious for hypothalamic-pituitary abnormality include midline facial dysmorphology, hypoglycemia, micropenis or visual abnormalities eg nystagmus.
- Transient hypothyroxinemia of prematurity, caused by immaturity of HPA axis can result in low T4 levels.
- Congenital hypothyroidism may be multifactorial, and may be primary or secondary.
- In Primary Hypothyroidism (thyroid failure, often defect in thyroid gland formation or defect in hormone biosynthesis), FT4 is low or normal; TSH is elevated. **MOST COMMON**
- In Central Hypothyroidism (pituitary/hypothalamic cause), FT4 is low but TSH may be normal or low (rare).
- Total and Free T3 are generally not necessary for screening and monitoring.
- Thyroid Imaging (Ultrasonography or scintigraphy) is sometimes performed but **should never delay initiation of LT4 therapy**

Treatment

Treatment of hypothyroidism includes thyroid hormone replacement (Levothyroxine; LT4). **Treatment should be started immediately (definitely within 2 weeks of birth) for optimal neurodevelopmental outcome**, and infants should be rendered euthyroid as promptly as possible. Brand-name thyroid hormone (i.e., Synthroid, Levoxyl, Unithroid) is an equivalent option for therapy as is generic LT4. Switching of levothyroxine from brand name to generic preparations, or between generic preparations can lead to perturbations in serum TSH, and is not recommended unless under close supervision of endocrinologist. Pharmacy prepared suspensions are not recommended. In addition, other forms of thyroid hormone replacement, such as desiccated porcine thyroid hormone (Armour Thyroid, Nature-Throid), are not well studied for use in hypothyroidism in neonates and children, and is not recommended.

Dosing of LT4 is in micrograms, and pill strengths are commonly color-coded for ease of use and safety. Initial dosing in congenital hypothyroidism is 10-15 mcg/kg/day dosed once daily (usually 37.5 mcg or 50 mcg in term infant).
Administration along with some foods and supplements, such as soy and high fiber, should be avoided as it can impair LT4 absorption. Titration of doses is by serial thyroid function testing (TSH, Free T4), generally done about 6-8 weeks after a dose change, and even more frequently in neonates. Follow-up visits with Endocrinology is recommended at frequent regular intervals to monitor adherence, blood levels, and growth and development. Adequate education of parents on proper administration of medication by trained personnel is highly desirable.

Suggested References and Additional Reading

- American Academy of Pediatrics, Rose SR; Section on Endocrinology and Committee on Genetics, American Thyroid Association, Brown RS; Public Health Committee, Lawson Wilkins Pediatric Endocrine Society, Foley T, Kaplowitz PB, Kaye CI, Sundararajan S, Varma SK. Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics. 2006 Jun;117(6):2290-303.
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- Juliane Léger, Antonella Olivieri, Malcolm Donaldson, Toni Torresani, Heiko Krude, Guy van Vliet, Michel Polak, Gary Butler. On behalf of ESPE-PES-SLEP-JSPE-APEG-APPES-ISPAE, and the Congenital Hypothyroidism, Consensus Conference Group, European Society for Paediatric Endocrinology. Consensus Guidelines on Screening, Diagnosis, and Management of Congenital Hypothyroidism. Horm Res Paediatr 2014;81:80–103

- U.S. Food and Drug Administration's Decision Regarding Bioequivalence of Levothyroxine Sodium. American Thyroid Association, The Endocrine Society, and American Association of Clinical Endocrinologists. B Thyroid. July 2004, Vol. 14, No. 7: 486-486.
- Irwin Klein and Sara Danzi. Evaluation of the Therapeutic Efficacy of Different Levothyroxine Preparations in the Treatment of Human Thyroid Disease. Thyroid. December 2003, Vol. 13, No. 12: 1127-1132

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