

45. Screening for Congenital Hypothyroidism

RECOMMENDATION

Screening for congenital hypothyroidism with thyroid function tests on dried-blood spot specimens is recommended for all newborns in the first week of life (see *Clinical Intervention*).

Burden of Suffering

In the U.S., congenital hypothyroidism occurs in 1 of 3,600–4,000 infants.^{1,2} Clinical diagnosis occurs in <5% of newborns with hypothyroidism because symptoms and signs are often minimal.¹ Without prompt treatment, most affected children gradually develop growth failure, irreversible mental retardation, and a variety of neuropsychologic deficits, comprising the syndrome of cretinism.^{1,2} These complications have become rare since the introduction in the 1970s of routine neonatal screening and early treatment of congenital hypothyroidism.

Accuracy of Screening Tests

In the U.S., screening for congenital hypothyroidism in neonates is almost always done by the radioimmunoassay of serum thyroxine (T_4) and thyroid-stimulating hormone (TSH) from dried-blood spot specimens collected by heelstick and adsorbed onto filter paper.^{3,4} Laboratories in most of the U.S. measure T_4 on all specimens, and TSH only if the T_4 level is low; in several states, most of Europe, and elsewhere in the world, TSH is the initial screening test.^{3,5} Simultaneous measurement of both T_4 and TSH has greater sensitivity for congenital hypothyroidism than either of the two sequential methods currently used,⁶ but it is not considered cost-effective by most programs at this time.^{5,7} The T_4 assay appears to have greater precision and reproducibility than the TSH assay, but false-negative rates are similar with the two methods.⁶ Both types of screening may miss the 3–5% of cases of congenital hypothyroidism that are caused by pituitary dysfunction, as well as the 3–14% of cases in which patients present with hypothyroxinemia and delayed TSH elevation.^{8–10} The primary T_4 -supplemental TSH approach also misses some patients with residual thyroid tissue (i.e., ectopic gland) that results in initially normal T_4

with elevated TSH; sensitivity for these cases can be improved by repeat screening at 2–6 weeks.¹¹ Using a higher cutoff point to define abnormal T_4 results in fewer false negatives due to these biologic factors. In one population, using a cutoff of the lowest 5% of T_4 values to define “low” missed 3.5% of cases, whereas using the lowest 10% resulted in 1.5% being missed.¹² Only 0.2% of cases were missed using the lowest 20% as a cutoff, but at substantially increased cost in terms of repeat testing.

False negatives also occur due to screening errors. Such failures occur in specimen collection, laboratory procedures (e.g., failure to record an abnormal result), or follow-up.¹³ Standards for adequate blood collection on filter paper for neonatal screening programs have been published.^{13a} Infants at increased risk for false negatives from screening errors include those born at home, ill at birth, or transferred between hospitals early in life.² In North America, an estimated 6–12% of neonates with congenital hypothyroidism are not detected in screening programs as a result of biologic factors or screening errors.^{8,13}

In established U.S. screening programs, there are 4–8 false positives for every proven case,⁸ although follow-up testing readily corrects these. Screening with primary TSH instead of T_4 -supplemental TSH may result in fewer false-positive tests.^{8,14} False-positive results are more likely when screening is done in the first 24–48 hours of life, since normal TSH values in the first 2 days of life may exceed the standard cutoff used by most programs.¹⁵ Evidence for long-term adverse psychologic effects from falsely positive screening test results is limited by methodologic flaws.^{16–19}

Effectiveness of Early Detection

Most cases of congenital hypothyroidism present clinically during the first year of life.²⁰ Retrospective studies of patients with congenital hypothyroidism have reported that delay of diagnosis and treatment beyond the first 1–3 months of life is likely to result in irreversible neuropsychologic deficits.^{21–25} More recent prospective studies show that screening neonates and treating affected infants within the first weeks of life results, on average, in normal or near-normal intellectual performance and growth at ages 5–12 years.^{26–34} These children appear to have somewhat lower cognitive and motor development compared to sibling or classmate controls, however, and continue to manifest subtle deficits in language, perception, and motor skills.^{27,28,31–35} Both age at onset of therapy and quality of therapeutic control achieved during the first year of life affect long-term intellectual outcome, supportive evidence for a benefit from earlier detection and treatment.^{27,28,31–33,35} The reduced incidence of severe neuropsychologic effects observed with early, adequate treatment has prompted most Western governments to require routine screening for all neonates.

Screening at birth may, in fact, occur too late to prevent important

neurodevelopmental deficits in some infants. Observational studies suggest that infants affected more severely in utero, as evidenced by greater delay in bone age at diagnosis, lower T_4 at screening, or a diagnosis of thyroid agenesis, have significantly poorer developmental outcomes compared to those with milder disease or to normal controls, even when detected and treated in the newborn period.^{28,31-36}

Recommendations of Other Groups

Screening of newborns for hypothyroidism is offered in all states, but mandated in 46 states and the District of Columbia.³ Five states and the District of Columbia require or strongly recommend a routine second screening test, from 1 to 4 weeks later.³ Screening is recommended by the Canadian Task Force on the Periodic Health Examination,⁷ the American Academy of Family Physicians,³⁸ Bright Futures,³⁹ and jointly by the American Academy of Pediatrics and the American Thyroid Association.⁵

Discussion

The natural history of congenital hypothyroidism has changed dramatically since newborn screening was instituted in this country.² Before screening was available, many children with this disorder were at least moderately, and sometimes profoundly, retarded, while recent prospective studies have demonstrated normal or near-normal intelligence in virtually all of those detected by screening and treated early in life. There is thus good evidence to support screening for congenital hypothyroidism in the newborn.

CLINICAL INTERVENTION

Screening for congenital hypothyroidism with thyroid function tests performed on dried-blood spot specimens is recommended for all newborns, optimally between days 2 and 6, but in all cases before newborn nursery discharge ("A" recommendation). Blood specimens should be collected by heelstick, adsorbed onto filter paper, and air dried using standard technique.^{13a} The choice of which thyroid function test or tests to perform is generally determined by individual state requirements.³ Testing procedures and follow-up treatment for abnormal results should follow current guidelines.⁵ Care should be taken to ensure that those born at home, ill at birth, or transferred between hospitals in the first week of life are appropriately screened before 7 days of age. Normal newborn screening results should not preclude appropriate evaluation of infants presenting with clinical symptoms and signs suggestive of hypothyroidism.

The draft update of this chapter was prepared for the U.S. Preventive Services Task Force by Carolyn DiGuseppi, MD, MPH.

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