

CLINICAL INQUIRIES

From the
Family Physicians
Inquiries Network

What are the causes of elevated TSH in a newborn?

Evidence-based answer

Congenital hypothyroidism is a critical cause of elevated thyroid-stimulating hormone (TSH) in newborns; evaluate all neonates with an elevated TSH for congenital hypothyroidism (strength of recommendation [SOR]: **A**).

Other causes of an elevated TSH include transient hypothyroidism due to neonatal illness, prematurity, iodine excess or deficiency, and maternal medication or maternal thyroid disease.

Clinical commentary

Another cause of elevated TSH?

Drawing the TSH too early

I practice in a state that screens newborns using TSH levels instead of T4 levels. In my experience, the most common reason for an elevated TSH is that the metabolic screen was drawn too early, before the initial physiologic peak after birth has returned to the screening cutoff level. In these cases, a repeat TSH is almost

always normal.

However, there have been several children with transient hypothyroidism that I have seen over the years with mild TSH elevations on repeat testing. The developmental implications for the infant are serious enough in these children to warrant endocrinology follow-up.

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Evidence summary

Feeding difficulties, inadequate weight gain, and unusual physical exam findings may lead providers to assess thyroid function in newborns. Additionally, while measurement of free T4 is more common, some states use TSH as the required newborn screening assay to evaluate for congenital hypothyroidism. Whether ordered as a screening test or in response to symptoms, an elevated TSH in a newborn requires further investigation.

Congenital hypothyroidism is the most serious cause of an elevated TSH in a newborn. If left untreated, congeni-

tal hypothyroidism leads to developmental delay and mental retardation; however, with early treatment, intellectual outcomes are greatly improved. Newborns with an elevated TSH should be evaluated with repeat TSH and free T4 measurements in order to assess for congenital hypothyroidism.

TSH >50 mU/L increases chances of congenital hypothyroidism

Not surprisingly, higher levels of TSH increase the likelihood of congenital hypothyroidism. A study from the Netherlands examined diagnoses of infants with an increased TSH

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FAST TRACK

All neonates with high TSH should be evaluated for congenital hypothyroidism

Common causes of elevated TSH in newborns

- Congenital hypothyroidism
- Transient hypothyroidism due to neonatal illness
- Prematurity
- Iodine excess or deficiency
- Improper screening technique
- Incorrect normal result intervals for age
- Maternal medication or maternal thyroid disease



FAST TRACK

Other common causes of elevated TSH include prematurity, severe illness, and errors in the screening procedure

on newborn screening heelstick. Of 112 newborns with a TSH >50 mU/L, 110 (98%) had congenital hypothyroidism on further examination. However, only 34 of 594 (5.7%) newborns with a TSH between 9 and 20 mU/L were diagnosed with congenital hypothyroidism. Nineteen of 46 newborns (41%) with levels between 20 and 50 mU/L had congenital hypothyroidism.¹

Other common causes of hypothyroidism

While TSH is generally an accurate measurement of thyroid function, other factors can also lead to an elevated level. The same Dutch study mentioned above explored the presumed causes of elevated TSH among children who were diagnosed with transient hypothyroidism (initially elevated TSH level found to be normal on follow-up testing). The most common causes were thyroid-binding globulin deficiency (200/548 or 36% of newborns

with transient hypothyroidism), severe illness (36%), prematurity (8%), and errors in screening procedures (4%).

Another study confirmed that TSH levels were higher in infants born preterm; babies with the earliest gestational ages had the highest TSH levels. The same study also found that TSH levels increased with increasing degrees of illness. Very preterm babies, those with cerebral pathology, low Apgar scores, respiratory distress syndrome, persistent ductus arteriosus requiring treatment, and necrotizing enterocolitis were at highest risk for having abnormally elevated TSH levels in this study.² If a sample is drawn from a newborn exhibiting symptoms (such as poor feeding or hypotonia), the TSH level may be elevated in spite of normal thyroid function.

Maternal thyroid disease can also cause a suppression of thyroid function in the newborn. One study¹ found that of 34 children with transient hypothyroidism, 10 had mothers with undertreated or unrecognized Graves disease.

Finally, either iodine excess or iodine deficiency can cause transient hypothyroidism. Case reports have directly demonstrated the effects of topical iodine exposure on newborn TSH levels.³⁻⁵ Deficiency of dietary iodine is a common cause of both congenital and transient hypothyroidism in newborns worldwide, although it is rare in the United States. The World Health Organization lists 54 countries with inadequate iodine intake; consider children from these countries at high risk for hypothyroidism due to iodine deficiency.⁶

Draw TSH on the second or third day of life

In term, healthy newborns, TSH levels normally increase to levels of 60 mU/L within 30 minutes of delivery. This is followed by a rapid decline in TSH levels over the first 5 days of life to <10 mU/L. An Australian study found more elevated TSH levels for samples drawn on day 2 of life compared with day 3 of life, likely

reflecting normal postnatal physiology.³ Age-specific reference ranges are necessary for interpretation of TSH levels during the first 5 days of life. The second or third day of life remains the optimal time for screening when appropriate reference ranges are used.

Recommendations from others

The United States Preventive Services Task Force (USPSTF),⁷ the American Academy of Family Physicians,⁸ the American Academy of Pediatrics,⁹ and the American Thyroid Association (ATA)¹⁰ all recommend routine screening of asymptomatic newborns for congenital hypothyroidism. The USPSTF recommends that clinicians evaluate abnormal thyroid screening results with a supplemental lab test, using TSH as the primary test and T4 as the supplemental test.⁷ Additionally, the ATA endorses a second thyroid screening at 7 to 14 days of life to increase specificity of congenital hypothyroidism screening.¹⁰ ■

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