HYPOTHYROIDISM, CONGENITAL
Supporting information

This guideline has been prepared with reference to the following:

Public Health England. Laboratory guide to screening for CHT in the UK. 2020. London. PHE

https://www.gov.uk/government/publications/congenital-hypothyroidism-screening-laboratory-handbook/a-laboratory-guide-to-newborn-blood-spot-screening-in-the-uk-for-congenital-hypothyroidism#pre-term

NICE. Thyroid disease: assessment and management. 2019. NICE. London

https://www.nice.org.uk/guidance/ng145

Association for Clinical Biochemistry. UK guidelines for the use of thyroid function tests. 2006. London. ACB

https://www.british-thyroid-association.org/sandbox/bta2016/uk_guidelines_for_the_use_of_thyroid_function_tests.pdf

Rose SR, Brown RS, Foley T, et al. Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics 2006;117:2290-303

http://pediatrics.aappublications.org/content/117/6/2290.full

Screening

In preterm infants, blood testing should be performed on day 6 and repeated at 36-40 weeks gestational age?
Revised UK guidelines published in April 2006 (see above) made this recommendation, but with the proviso that it should be kept under review. A study (Korada, 2008) compared baseline readings of thyroid stimulating hormone (TSH) in 2238 preterm infants with second samples taken from 2039 infants. No infant with a normal TSH concentration on first sampling was found to have a reading of > 10mU/l on second sampling. The authors concluded that repeat sampling may not be required with a lower screening threshold of 6 mU/l.

Korada M, Pearce MS, Ward Platt MP, et al. Repeat testing for congenital hypothyroidism in preterm infants is unnecessary with an appropriate thyroid stimulating hormone threshold. Arch Dis Child Fetal Neonatal Ed 2008;93:F286-8
http://fn.bmj.com/content/93/4/F286.long

Evidence Level: IV

Immediate management

Infants with congenital hypothyroidism have an increased incidence of other abnormalities?
A study of registry data in the US (Kumar, 2009) showed that cchildren with congenital hypothyroidism had a significantly increased risk of congenital renal and urological anomalies (OR 13.2; 95% CI 10.6-16.5). The other significantly increased defects in congenital hypothyroidism were cardiac, gastrointestinal, and skeletal. Analysis of matched data confirmed an increase of congenital renal and urologic anomalies (OR 4.8; 95% CI 3.7-6.3).

Kumar J, Gordillo R, Kaskel FJ, et al. Increased prevalence of renal and urinary tract anomalies in children with congenital hypothyroidism. J Pediatr 2009;154:263-6
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3749842/

Evidence Level: IV

Treatment

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A starting dose of 10 mcg/kg/d of thyroxine is appropriate? Do higher dose regimens result in adverse effects on memory, attention or behaviour?

"What constitutes optimal TH therapy is not yet certain" (Rose, 2006). This dose is at the lower end of the range recommended by current American Academy of Pediatrics guidelines (Rose, 2006). These advise a starting dose of 10-15 mcg/kg/d, depending on the severity of the initial hypothyroidism. When a higher starting dose (12-17 mcg/kg/d) is used, serum T_4 normalises in 3 days and TSH returns to the target range within 2 weeks (Bakkar, 2002). However, "evaluation of cognitive outcome is important after use of this increased dose" (Rose, 2006).

A cohort based follow up study of 49 young adults with early treated congenital hypothyroidism compared these with 41 matched sibling controls (Oerbeck, 2005). At age 20, those subjects given high dose (>/= 7.8 mcg/kg/d) therapy displayed no adverse effects on higher order cognitive skills, compared to those on low dose (<7.8 mcg/kg/d) treatment. The high dose group did, however, exhibit significant differences on some measures of memory, attention (distractibility) and behaviour. The authors concluded that their findings supported the use of higher dose treatment, but acknowledged that only 12 of their 49 subjects had been given doses of >10 mcg/kg/d, and that "definite answers to the outcome in high dose treatment groups await further studies".

The largest study to date looking at these outcomes was a systematic review of 14 cohort studies in 1321 patients (Hrytsiuk, 2002).This concluded that "The evidence for an effect of starting dose…on cognitive development, growth, or behavior is too weak to justify recommendations in favor of high- or standard-dose regimens."

The most severely hypothyroid infants are at risk for a 5-20 point decrease in IQ, and may benefit from a starting dose of 12-17 mcg/kg/d (LaFranchi, 2007).

A Cochrane Systematic Review of a single trial in 47 infants (Ng, 2009) concluded that there was insufficient evidence with which to answer this question.

Bakkar B, Kempers MJ, DeVijlder JJ, et al. Dynamics of the plasma concentrations of TSH, FT4 and T3 following thyroxine supplementation in congenital hypothyroidism. Clin Endocrinol 2002;57:529-37

Hrytsiuk I, Gilbert R, Logan S, et al. Starting dose of levothyroxine for the treatment of congenital hypothyroidism: a systematic review. Arch Pediatr Adolesc Med 2002;156:485-91
http://archpedi.jamanetwork.com/article.aspx?articleid=191868

LaFranchi SH, Austin J. How should we be treating children with congenital hypothyroidism? J Pediatr Endocrinol Metab 2007;20:559-78

Ng SM, Anand D, Weindling AM. High versus low dose of initial thyroid hormone replacement for congenital hypothyroidism. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD006972
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006972.pub2/full

Oerbeck B, Sundet K, Kase BF, et al. Congenital hypothyroidism: no adverse effects of high dose thyroxine treatment on adult memory, attention, and behaviour. Arch Dis Child 2005;90:132-7
http://adc.bmj.com/content/90/2/132.long

Rose SR, Brown RS, Foley T, et al. Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics 2006;117:2290-303
http://pediatrics.aappublications.org/content/117/6/2290.full

Evidence Level: III

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