HYPOTHYROIDISM, CONGENITAL

This guideline and supporting nformation has been prepared with reference to the following:

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

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).

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

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

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

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

Evidence Level: III