

CONGENITAL HYPOTHYROIDISM

Introduction

The incidence of congenital hypothyroidism worldwide is 1 in 2500 - 4000 live births. In Malaysia, it is reported as 1 in 3666. It is the commonest preventable cause of mental retardation in children.

Thyroid hormones are crucial for: -

- normal growth and development of the brain and intellectual function, during the prenatal and early postnatal period
- maturation of the foetal lungs and bones

Clinical diagnosis

Most infants are asymptomatic at birth.

Subtle clinical features include :

- prolonged neonatal jaundice
- constipation
- a quiet baby
- enlarged fontanelle
- respiratory distress with feeding
- absence of one or both epiphyses on X-ray of left knee (lateral view)

If left untreated, overt clinical signs will appear by 3 - 6 months: coarse facies, dry skin, macroglossia, hoarse cry, umbilical hernia, lethargy, slow movement, hypotonia and delayed developmental milestones.

Most infants with the disease have no obvious clinical manifestations at birth, therefore neonatal screening of thyroid function should be performed on all newborns.

Treatment

Timing

- should begin immediately after diagnosis is established. If features of hypothyroidism are present, treatment is started urgently.

Duration

- treatment is life long except in children suspected of having transient hypothyroidism where re-evaluation is done at 3 years of age.

Preparation

- there are currently no approved liquid preparations
- only L-thyroxine *tablets* should be used. The L-thyroxine tablet should be crushed, mixed with breast milk, formula, or water and fed to the infant.
- the tablets should not be mixed with soy formulas or any preparation containing iron (formulas or vitamins), both of which reduce the absorption of T4

Table 1. Doses of L- thyroxine by age

Age	mcg/kg/dose, daily
0 - 3 months	10 - 15
3 - 6 months	8 - 10
6 - 12 months	6 - 8
1 - 5 yr	5 - 6
6 - 12 yr	4 - 5
> 12 yr	2 - 3

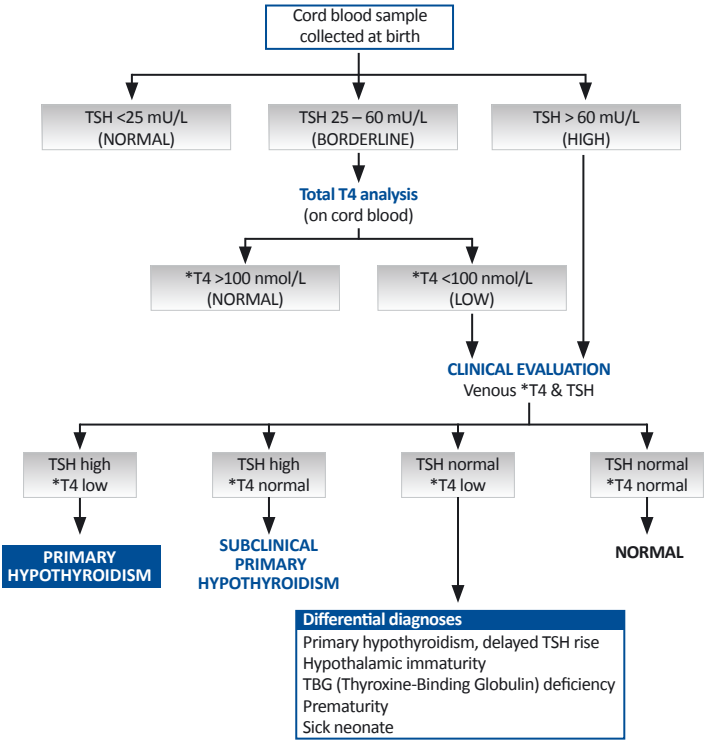
Note:

- average adult dose is 1.6 mcg /kg/day in a 70-kg adult (wide range of dose from 50 - 200 mcg/day).
- L-thyroxine can be given at different doses on alternate days, e.g. 50 mcg given on even days and 75 mcg on odd days will give an average dose of 62.5 mcg/day.

Table 1. Aetiology

<i>Thyroid dysgenesis</i> (85%)
athyreosis (30%)
hypoplasia (10%)
ectopic thyroid (60%)
<i>Other causes</i> (15%)
inborn error of thyroid hormone synthesis (1:30,000)
hypothalamo-pituitary defect (1:100,000)
peripheral resistance to thyroid hormone (very rare)
transient neonatal hypothyroidism (1:100 - 50,000)
endemic cretinism

Figure 1. Screening for congenital hypothyroidism



Interpretation of the results should take into account the physiological variations of the hormone levels during the neonatal period.

*Free thyroxine level if available is preferable to total thyroxine level.

Goals of therapy

- to restore the euthyroid state by maintaining a normal serum T4/ FT4 level at the upper half of the normal age-related reference range. Ideally, serum TSH levels should be between 0.5-2.0 mU/L.
- serum T4/ FT4 level usually normalized within 1-2 weeks, and then TSH usually become normal after 1 month of treatment
- some infants may continue to have high serum TSH concentration (10 - 20 mU/L) despite normal serum T4 values due to resetting of the pituitary-thyroid feedback threshold

Table 2. Goals of therapy in the first year of life

	Adequate treatment	Inadequate treatment
T4	10 -16 mcg/dL (130 - 206 nmol/L)	T4 < 10 mcg/dL (<103 nmol/L)
FT4	1.4 – 2.3 ng/dL (18 - 30 pmol/L)	
TSH	< 5 mU/L	TSH >15 mU/L more than once in first year

Follow-up

Monitor growth parameters and developmental assessment.

The recommended measurements of serum T4 / FT4 and TSH by American Academy of Pediatrics are according to the following schedules: -

- at 2 and 4 weeks after initiation of T4 treatment
- every 1 to 2 months during the first 6 months of life
- every 3 to 4 months between 6 months and 3 years of age
- every 6 to 12 months thereafter until growth is completed
- after 4 weeks if medication is adjusted
- at more frequent interval when compliance is questioned or abnormal values are obtained
- ongoing counseling of parents is important because of the serious consequences of poor compliance

Re-evaluation of patients likely having transient hypothyroidism

This is best done at age 3 years as most thyroid dependent brain growth is completed at this age.

- stop L-thyroxine for 4 weeks then repeat thyroid function test: T4 / FT4, TSH
- imaging studies: Thyroid scan, Ultrasound of the thyroid
- if the FT4 is low and the TSH value is elevated, permanent hypothyroidism is confirmed and L-thyroxine therapy should be re-instituted

Babies born to mothers with thyroid disorders

All newborns of mothers with thyroid diseases should be evaluated for thyroid dysfunction, followed up and treated if necessary.