Serum thyroxine and thyroid stimulating hormone concentrations after treatment of congenital hypothyroidism

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SUMMARY Serum thyroid stimulating hormone and thyroxine concentrations were monitored in 42 infants who had been treated for congenital hypothyroidism. Serum thyroid stimulating hormone concentrations were raised in 22 of the infants (52%) at 2 to 4 months, in 16 (38%) at 5 to 11 months, in 14 (33%) at 12 to 18 months, and in eight (19%) at 2 to 4 years. Serum thyroxine and the dose of L-thyroxine/kg/body weight were significantly lower in those infants with raised thyroid stimulating hormone concentrations. Thyroid stimulating hormone was appropriately suppressed when the dose of L-thyroxine was increased, and only one child had delayed maturation of the hypothalamic/pituitary/thyroid axis. We believe it is the infant’s rapid gain in weight in the first two years of life that necessitates this decrease in the dose of L-thyroxine/kg body weight and recommend that the treatment of this age group is reviewed every two to three months.

Screening programmes for congenital hypothyroidism were first reported in 19751,2 and are now practised in many countries. Initial reports confirmed their efficacy and detailed the children’s normal growth and development,3–5 though recent studies have suggested that these children may not perform as well as normal controls.6–8 This may reflect inadequate treatment and it is unfortunate that there are few reports9–11 and only one longitudinal study12 that have examined the serum thyroxine concentrations after treatment.

We now report plasma thyroid stimulating hormone and thyroxine concentrations after replacement treatment in children detected in the congenital hypothyroid screening programme in the South West region of England between 1981 and 1986. We have correlated these concentrations with the dose of L-thyroxine/kg body weight in an attempt to calculate optimal dosage regimens.

Patients and methods

The infants screened were those born in the South West region of England from 1981 to 1986. Capillary blood samples for the measurement of thyroid stimulating hormone were collected in duplicate on filter paper when babies were 7 days old and sent to the regional screening laboratory at Southmead Hospital, Bristol. Thyroid stimulating hormone was measured by an immunoradiometric assay (sensitivity 8 mU/l, interassay variation 12%). A blood spot thyroid stimulating hormone concentration of <25 mU/l was regarded as normal; a concentration of >80 mU/l was considered abnormal and infants were referred to a local paediatrician for clinical assessment and further biochemical investigations. Repeat blood spots were requested on neonates whose blood spot thyroid stimulating hormone concentrations were in the range 25 to 80 mU/l. If the blood spot thyroid stimulating hormone was >25 mU/l on repeat analysis the infant was referred to a local paediatrician for further investigations. The Medical Research Council definition of congenital hypothyroidism was adopted. This comprises a plasma or serum total thyroxine concentration by quantitative analysis of less than 65 nmol/l, or a plasma or serum thyroid stimulating hormone concentration by quantitative analysis of more than 10 mU/l.

Treatment with L-thyroxine and the children’s progress were supervised by the local paediatricians. Treatment was monitored by the filter paper capi-
lary blood assay for thyroid stimulating hormone. If
the blood spot thyroid stimulating hormone concen-
trations were higher than the detection limit of the
assay (8 mU/l), paediatricians were advised to check
the plasma or serum concentrations of thyroxine and
thyroid stimulating hormone.
We identified through the screening laboratory all
children with raised serum or plasma thyroid stimu-
"lating hormone concentrations (that is, >10 mU/l)
and extracted clinical and biochemical data and
treatment regimens from their hospital case notes.
The data were analysed by comparing those with
raised plasma thyroid stimulating hormone concen-
trations with those with normal concentrations.
Comparison of the serum thyroxine concentrations
and doses of L-thyroxine between the two groups
was by the Mann-Whitney test and Student’s t test,
respectively. Statistical analysis was done of the
pooled results and of the results at different ages.

Results

The population of the south west of England is
roughly three million, and the annual birth rate
about 37 000, and 185 723 infants (99% of all
newborn babies) were screened between 1981 and
1986. The recall rate for a repeat sample was 0.11%.
Forty two infants (16 boys and 26 girls) had
primary congenital hypothyroidism according to the
Medical Research Council definition. The incidence
is 1:4400. Seven other infants (five boys, two girls)
had raised plasma thyroid stimulating hormone
concentrations and total thyroxine concentrations
within the normal range (all were more than
100 nmol/l). Three have subsequently become
hypothyroid (unpublished observations).

The mean age at diagnosis was 13.8 days (range
9–18), that at starting treatment was 16 days (range
9–38), and that at the time of study was 31.5 months
(range 6–63).

After treatment the serum thyroid stimulating
hormone concentrations were raised in 22 of the
infants (52%) between 2 and 4 months, in 16 (38%)
between 5 and 11 months, in 14 (33%) between 12
and 18 months, and in eight (19%) between 2 and 4
years. Serum thyroxine concentrations were never
below the normal range for age throughout the
study period but were significantly lower in the
infants with raised thyroid stimulating hormone
congenital hypothyroidism. Serum thyroxine concen-
trations were 1369 nmol/l (range 100–2500).
Of these, one infant had persistently raised thyroid
stimulating hormone concentrations in the presence
of serum thyroxine concentrations in the upper part
of the normal range and a satisfactory thyroxine
dose/kg body weight (described as 'delayed matu-
aration' in the figures). In all other instances thyroid

![Graph](attachment:fig1.png)

Fig 1 Serum thyroxine concentrations in children with normal or raised thyroid stimulating hormone.
Table Mean serum thyroxine concentrations (nmol/l) in children with normal or raised thyroid stimulating hormone (TSH) concentrations during the study

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean TSH concentration (mU/l)</th>
<th>&lt;10</th>
<th>≥10</th>
</tr>
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<tbody>
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<td></td>
<td>165</td>
<td>120</td>
</tr>
<tr>
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<td></td>
<td>198</td>
<td>111</td>
</tr>
<tr>
<td>0.75</td>
<td></td>
<td>148</td>
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</tr>
<tr>
<td>4</td>
<td></td>
<td>159</td>
<td>128</td>
</tr>
</tbody>
</table>

stimulating hormone was normally reduced when the dose of L-thyroxine was appropriately increased.

The dose of L-thyroxine/kg body weight varied widely at all ages throughout the study period but this was most pronounced in early infancy. The mean L-thyroxine doses/kg body weight were significantly lower in infants with raised thyroid stimulating hormone concentrations (p<0.0001) (fig 2).

The growth and development of all the children were recorded as normal.

Discussion

Our results confirm those of earlier studies that showed that serum thyroid stimulating hormone concentrations remain raised in a number of children who have been treated for congenital hypothyroidism. 9 10 11 12

The only study comparable with our own12 reported that one third of 36 infants treated for congenital hypothyroidism had raised serum thyroid stimulating hormone concentrations at 1 year of age. The authors observed that those children with raised thyroid stimulating hormone concentrations had lower serum thyroxine concentrations and had received lower doses of L-thyroxine/kg body weight. They suggested that the raised thyroid stimulating hormone concentrations was due either to an alteration in the set point of reduction, or to under treatment.

Other reports are less comprehensive. Sato et al6 studied nine children with athyrotic or ectopic hypothyroidism diagnosed between 6 months and 17 years of age. They defined euthyroidism as a basal thyroid stimulating hormone concentration of <10 mU/l and a normal thyroid stimulating hormone response to thyrotrophin releasing hormone, and concluded that the pituitary threshold for regulation of thyroid stimulating hormone release by thyroxine is higher in infants and young children, and gradually decreases over several years. They recommended that the dose of L-thyroxine/kg body weight should be comparatively higher in infancy and decrease through childhood.

Schultz et al10 reported five infants with congenital hypothyroidism and persistently raised thyroid stimulating hormone concentrations up to 24 months of age. The dose of L-thyroxine was appropriate, though in the lower half of the recommended range for age in four of the infants, and inadequate in the fifth. Serum thyroxine was measured on 34 occasions and all but one were within the lower range of normal. Thyroid stimulating hormone was normally reduced in four infants when their serum thyroxine concentrations rose into the upper range of normal. Schultz et al suggested that the hypothalamic/pituitary threshold for reduction of thyroid stimulating hormone is unusually high in infancy and their data confirm the need for serum thyroxine to be kept in the upper range of normal.

Our results show that although serum thyroxine concentrations were within the normal range for age for all the children, there was a negative correlation between their serum thyroid stimulating hormone and thyroxine concentrations and their serum thyroid stimulating hormone and thyroxine dose when expressed by kilogram body weight. Individually, when their thyroxine doses were increased their serum thyroid stimulating hormone concentrations were normally reduced. We believe that it is the infants' rapid increase in body weight that provokes...
Serum thyroxine and thyroid stimulating hormone concentrations

We thank the paediatricians in the South West region for their help.

References


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Accepted 14 June 1988
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Arch Dis Child 1988 63: 1368-1371
doi: 10.1136/adc.63.11.1368

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