Summary

The serum concentrations of tri-iodothyronine (T₃), thyroxine (T₄), and thyrotrophin (TSH) were measured in 10 term newborn infants between birth and the age of 2 days by radioimmunoassay. The mean concentration of T₃ in maternal serum was 1.62 μg/l, and it increased from the low cord blood level of 0.63 μg/l to the peak value of 1.76 μg/l within the first 2 hours of life. Mean serum T₄ concentrations increased from the cord blood level of 145 μg/l to the peak value of 205 μg/l within the first 24 hours of life. The postnatal increase of the mean serum TSH concentrations from the cord blood level of 5.7 mU/l to the peak value of 20.6 mU/l within 2 hours was similar to the increase of T₃.

These data confirm earlier reports which show that T₃ secretion is low at birth and TSH secretion is stimulated strongly but transiently after birth, and that the low T₃ secretion is rapidly normalized in 2 hours along with the TSH release. Because of these strong and rapid changes, we recommend screening of the function of the pituitary-thyroid axis in neonates after the age of 24 hours.

REFERENCES


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Raised serum TSH in hypothyroidism

Hypothyroidism is a graded phenomenon; at one end of the spectrum the symptoms and clinical features are overt, at the other end they may be so mild as to escape clinical detection. In paediatric practice a good case can be made for the desirability of detecting early hypothyroidism of the mildest degree but hitherto lack of specific symptoms and the fact that conventional tests of thyroid function may be normal for a variable period of time have delayed the diagnosis.

Recently it has become possible to assay the serum thyroid stimulating hormone (TSH) concentration (Hall, 1972), and it is now accepted that patients with mild hypothyroidism have raised serum TSH. Conversely, thyroid insufficiency can be confidently excluded if the serum TSH concentration is normal.

Normal serum TSH values range from undetectable to 4 μU/ml (Hall and Evered, 1973) but since this is a relatively new assay, laboratories must determine the specificity and accuracy of the test in their hands as well as establish their range of normal values. There are, however, no significant differences in TSH levels in men, women, or children after the neonatal period. High values for serum TSH almost certainly reflect a reduction in the circulating levels of thyroxine (T₄) and triiodothyronine (T₃) but by an instant reciprocity the increased TSH output may maintain, at least for a time, T₄ and/or T₃ levels within the range which will prevent a state of overt hypothyroidism.

In this case report we draw attention to the importance of serum TSH assay when suspicion of hypothyroidism is aroused, even though conventional tests of thyroid function are normal.

Case report

A female (born 4 February 1968) is the second child of healthy unrelated parents. She presented in January 1970 at the age of 1-9 years because of shortness of stature. Since the age of 1 year the parents had been concerned because of her failure to grow. There was a history of constipation but no lethargy or preference for warm weather. Clinically (height 78 cm, weight 9·9 kg) she was small and alert and apart from fine sparse hair there were no other positive features of disease. Bone age was 1 year, epiphysial dysgenesis was absent, serum cholesterol was 169 mg/100 ml (4·mmol/l) and protein-bound iodine 6·0 μg/100 ml (472 nmol/l).

She was seen regularly during the following 18 months during which period constipation persisted and also growth failure. In June 1972 at the age of 2·4 years the serum cholesterol was 245 mg/100 ml (6·95 mmol/l),
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protein-bound iodine 7.8 μg/100 ml (615 nmol/l), and serum HGH level 64 ng/ml (insulin tolerance test at 30 min). X-ray of bones showed the bone age to be 1·1 years with epiphyseal irregularities at the hips and elbows suggestive of multiple epiphyseal dysplasia. In January 1973 further x-rays of the bones showed an extension of the lesion in the head of the right femur to cystic change and widening of the metaphysis. These features were interpreted as indicating Perthes’s disease of the right hip. Bone age was then 1·5 years. She was seen by an orthopaedic surgeon whose opinion was that Perthes’s disease in this age group had a good prognosis. Active interventional treatment did not seem to be indicated. In September 1973 and again in November 1973 the failure to gain height (97 cm) was striking, but her physical appearance did not suggest subthyroidism. ECG gave a normal tracing; there was no significant alteration in the appearances of the epiphyses beyond that already noted though the bone age was only 2 years (at age 5·75 years). Serum analysis, however, showed thyroxine 3·2 μg/100 ml (41·2 nmol/l), tri-iodothyronine 1·16 ng/ml (1·79 nmol/l), and TSH 310 μU/ml. Immunofluorescence test for antibody to thyroid microsomes was weakly positive.

Subsequent to these findings we confirmed by radioiodine studies that she had a small lingual thyroid with a gland uptake at 24 hours of 12·4% of the dose administered, and at 48 hours a total plasma 131I of 0·32% of the dose per litre. Hypothyroidism due to small lingual thyroid was therefore confirmed. She was given L-thyroxine sodium 0·05 mg daily for 10 days, followed by 0·1 mg daily for 6 months before increasing to 0·2 mg daily. The expected clinical response to L-thyroxine is being achieved. In the Table the early response to administered thyroxine is shown.

Discussion

Clinically overt hypothyroidism is confirmed by showing a reduced serum thyroxine concentration. Suspected and mild hypothyroidism may require the supportive evidence of an increased serum TSH concentration. Indeed serum TSH is the most sensitive index of thyroid failure, even in the face of normal serum values of T4 and T3. From the results shown in the Table it is clear that our patient was maintaining adequate serum T3 levels under intense TSH stimulation while the less metabolically active T4 was on the decline. Indeed, it seems probable that a diagnosis of hypothyroidism might have been reached at a much earlier age in our patient if TSH estimations had been available, and, in future, estimation of the serum TSH level with or without stimulation by thyroid releasing hormone (TRH) should form part of the routine investigation of every child in whom hypothyroidism may be a possibility. 6 days after beginning oral L-thyroxine at a very modest dosage level, the serum TSH level continued to be remarkably high even though the serum T4 and T3 levels were by then adequately high. By day 12 of

TABLE

<table>
<thead>
<tr>
<th>Date</th>
<th>Treatment</th>
<th>Total T4 in μg/100 ml (nmol/l)</th>
<th>Total T3 in ng/ml (nmol/l)</th>
<th>T3 resin uptake</th>
<th>TSH (μU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 Sept 73</td>
<td>No therapy</td>
<td>2-1 (27-0)</td>
<td>1-34 (2-06)</td>
<td>123</td>
<td>246</td>
</tr>
<tr>
<td>1 Nov 73</td>
<td>No therapy</td>
<td>3-2 (41-2)</td>
<td>1-16 (1-79)</td>
<td>124</td>
<td>310</td>
</tr>
<tr>
<td>21 Nov 73</td>
<td>T4 0-05 mg</td>
<td>6-0 (103)</td>
<td>1-68 (2-59)</td>
<td>113</td>
<td>230</td>
</tr>
<tr>
<td>27 Nov 73</td>
<td>T4 0-1 mg</td>
<td>12-4 (160)</td>
<td>1-90 (2-93)</td>
<td>95</td>
<td>16</td>
</tr>
<tr>
<td>11 Dec 73</td>
<td>'</td>
<td>13-0 (167)</td>
<td>2-34 (3-60)</td>
<td>98</td>
<td>1-1</td>
</tr>
<tr>
<td>20 Dec 73</td>
<td>'</td>
<td>14-8 (190)</td>
<td>2-0 (3-08)</td>
<td>92</td>
<td>UD</td>
</tr>
<tr>
<td>27 Dec 73</td>
<td>'</td>
<td>11-2 (144)</td>
<td>2-0 (3-08)</td>
<td>91</td>
<td>UD</td>
</tr>
<tr>
<td>4 Jan 74</td>
<td>'</td>
<td>14-4 (185)</td>
<td>2-0 (3-23)</td>
<td>84</td>
<td>UD</td>
</tr>
<tr>
<td>10 Jan 74</td>
<td>'</td>
<td>13-2 (170)</td>
<td>2-4 (3-70)</td>
<td>86</td>
<td>UD</td>
</tr>
<tr>
<td>28 Jan 74</td>
<td>'</td>
<td>14-8 (190)</td>
<td>1-8 (2-77)</td>
<td>80</td>
<td>UD</td>
</tr>
<tr>
<td>Normal adult range</td>
<td></td>
<td>4-3-11·2 (55-144)</td>
<td>0-6-1·8 (0-9-2·77)</td>
<td>90-120</td>
<td>UD-10</td>
</tr>
</tbody>
</table>

UD, undetectable,
treatment, serum T₂ and T₄ levels were in the high normal range, by which time the serum TSH level had fallen dramatically. Thereafter, with increasing serum T₃ and T₄ the serum TSH fell to persistently undetectable levels.

Most clinicians have their own dosage schedule of thyroxine for the treatment of hypothyroidism and hitherto have tended to judge dosage against satisfactory linear growth and osseous maturation. Additionally, on the basis of evidence that the developing brain and skeleton require more thyroxine than other tissues for adequate development (Hutchinson, 1969), it has been felt by some that it is advisable to keep serum T₃ and T₄ levels marginally above normal levels. While such high levels cannot completely reverse the intrauterine damage to the brain, it can be claimed that modestly high circulating levels of T₃ and T₄ ought to permit maximum brain growth and hopefully improve the ultimate IQ.

In patients with juvenile hypothyroidism there is perhaps less need for higher than normal T₃ and T₄ serum levels since intrauterine brain development is likely to have been normal. It is only the increasing systemic requirement for thyroid hormones beyond the capacity of the patient’s thyroid which induces clinical hypothyroidism. It might then be concluded that normal serum T₃ and T₄ levels would permit subsequent normal growth and development.

While it is known that increased circulating levels of cortisol suppress both corticotrophin and growth hormone (Franchimont and Libon, 1966), it is not known if persistent suppression of TSH with exogenous thyroxine results also in suppression of other trophic hormones. Certainly if this were so our experience suggests that any suppression that may occur is not liable to give rise to clinical features suggestive of a trophic hormone deficiency. However, it is clear that these relatively new tests have provided tools by which serum levels in response to the various regimens of thyroxine therapy may be monitored in future and when these are correlated with the clinical response (in growth, osseous maturation, and IQ) a greater degree of certainty will be permissible.

Summary

It is desirable to detect early hypothyroidism of the mildest degree even before conventional tests of thyroid function become abnormal. Serum TSH levels (normal: undetectable to 4 μU/ml) rise in patients with mild hypothyroidism long before serum T₃ and T₄ levels fall. In the patient described the serum TSH level was 310 μU/ml, while other tests of thyroid function gave normal results. After treatment with thyroxine, serum TSH returned to normal. It should now be accepted that patients with mild hypothyroidism have a raised serum TSH and that thyroid insufficiency can be confidently excluded if the serum TSH concentration is normal. It is thus important to assay serum TSH when suspicion of hypothyroidism is aroused.

We are indebted to Dr. J. G. Radcliffe, Regional Radioimmunoassay Laboratory, for undertaking analysis of many of the serum samples.

REFERENCES


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Neonatal respiratory failure due to myotonic dystrophy

The occurrence of myotonic dystrophy in the newborn causing extreme and generalized hypotonia, bilateral facial weakness, ptosis, bilateral talipes equinovarus, and feeding difficulties has been documented for more than a decade (Vanier, 1962). Respiratory difficulties, principally attacks of cyanosis associated with ineffective swallowing and pulmonary aspiration, have also been recorded (Dodge *et al.*, 1965). In the following case respiratory involvement was marked, and caused death within 2 days of birth.

Case report

The patient, a male weighing 2.95 kg was born at 37 weeks’ gestation by vaginal delivery. Before delivery hind water rupture had produced 4 l amniotic fluid. Immediate Apgar score was 8, but at 3 minutes the child became blue and limp, the cyanosis responding to airway aspiration and administration of 100% oxygen. Initial examination of the infant showed generalized
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