Early detection of congenital hypothyroidism

Congenital hypothyroidism, with an estimated incidence of 1 in 5–10,000 births, is probably the commonest endocrine disorder of early childhood. Its importance lies in the devastating effect which it can have on brain development, leading to subnormality and other manifestations such as clumsiness and hyperactivity. It is common experience that the condition is difficult or impossible to recognize during the first days or weeks after delivery. However, recent advances in laboratory methods, particularly thyrotrophin (TSH) and thyroxine (T4) assays, have opened up the possibility of screening for the disorder before the classical clinical picture develops. Studies on the feasibility of such screening are in progress in several centres. In this issue, Dr. Delange and his colleagues describe their experience at the Saint-Pierre Hospital, Brussels, using a radioimmunoassay to estimate plasma TSH on the 5th day of life. Their results, together with those reported from North America,1–3 clearly indicate that screening for congenital hypothyroidism is technically possible.

At first glance, the case for screening for congenital hypothyroidism seems clear. The poor prognosis for cases in which treatment has been very delayed has long been recognized and a number of studies have shown that the outlook is better in patients treated before the age of 3 months. There is less information on the outcome in cases treated soon after birth. In Table 1 we have summarized the available literature on cases treated at or before 6 weeks and on patients in whom treatment started between the ages of 7 and 12 weeks. Again, the results indicate that the prognosis is better with early treatment, particularly with regard to subnormality.

While all available evidence indicates that early recognition and treatment of congenital hypothyroidism will reduce the incidence and severity of later handicap, all the published series show wide overlap of intelligence in children treated early and late, and even in cases treated before 6 weeks the proportion with an IQ above 90 is less than expected (Table 1). This variation probably stems from differences in the timing and severity of thyroid deficiency in individual patients. It is widely accepted that the human placenta is impermeable to thyroid hormones but the effect of fetal hypothyroidism on brain growth is less clear. Experiments in animals have indicated that there are limited periods during which thyroid hormones are essential for normal brain development. For instance, cerebellar development is mainly postnatal in the rat and thyroid deficiency induced at birth produces abnormalities of myelination and dendritic connections.4 In the sheep this critical period begins during fetal life.5 Studies in children have shown that ataxia and clumsiness may be equally common in early- and late-treated cases.6 7 These findings, together with studies on intelligence, suggest that the thyroid-dependent period of brain growth in man may start before birth.

As we still do not know the relative importance of pre- and postnatal hypothyroidism on subsequent development we cannot fully assess the potential benefits of screening, and a multicentre study which compares the outcome in cases identified by screening or conventional methods will be necessary to clarify this point. In a limited screening programme in Quebec, the cost of identifying each case was roughly $4000 and it might be argued that precious resources could be better spent on selective investigation of 'at risk' cases. Congenital hypothyroidism is twice as common in girls and many cases are post-mature8. Although the classical features take weeks

<table>
<thead>
<tr>
<th>Age at start of treatment</th>
<th>No. of cases</th>
<th>IQ 90 or more</th>
<th>IQ 75 or less</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 w or earlier</td>
<td>18</td>
<td>55%</td>
<td>11%†</td>
</tr>
<tr>
<td>7–12 w</td>
<td>47</td>
<td>36%</td>
<td>38%</td>
</tr>
</tbody>
</table>


†2 cases classified as retarded but precise IQ not given.
or months to appear, symptoms are commonly present soon after birth. The significance of persistent jaundice is becoming more widely recognized but only one-third of cases show this feature (Table 2). Less impressive symptoms such as inactivity, difficulty in feeding, constipation, and slow weight gain are more common. All those responsible for the care of young infants, including midwives and health visitors, should be aware of the possible significance of such symptoms, as a higher index of suspicion could almost certainly lead to much earlier diagnosis in most cases. In suspected cases, estimation of TSH probably provides the most useful information. This test can usually be carried out on a capillary blood sample and a normal value of 5 μU/ml or less virtually excludes the diagnosis.

Estimation of plasma thyroidine can also be used to confirm or exclude hypothyroidism, but care must be taken to interpret results in the light of the high thyroidine levels normally found in early infancy.

Table 2. Frequency of hypothyroid symptoms within the first month.*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Lethargy</td>
<td>65%</td>
</tr>
<tr>
<td>Constipation</td>
<td>42%</td>
</tr>
<tr>
<td>Feeding difficulty</td>
<td>65%</td>
</tr>
<tr>
<td>Umbilical hernia</td>
<td>53%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>34%</td>
</tr>
<tr>
<td>Thick tongue</td>
<td>44%</td>
</tr>
</tbody>
</table>


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Addendum

Dussault et al. (1976) have recently described normal TSH levels in 3 out of 28 infants with plasma thyroxine values in the hypothyroid range. 2 of these infants appeared to have hypothalamic hypothyroidism. As such cases would not be detected by TSH screening, Dussault et al. (1976) recommend that plasma thyroxine assay is used to identify neonatal hypothyroidism.

Reference

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