and urine levels of total biopterin derivative (measured by Crithidia fasciculata assay) and an abnormal pattern of pterins on chromatography (Leeming et al., 1976). The results of the Crithidia assays carried out by one of us (R.J.L.) in 1975 on the patient of J. Bartholomé (Kaufman et al., 1975; Bartholomé et al., 1977) have not been published and we should like to present them (Table).

Table Levels of total biopterin derivative measured by Crithidia fasciculata assay in a patient with phenylketonuria (Bartholomé et al., 1977). Comparison with control values (mean ± SD)

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Serum (g/l)</th>
<th>Urine (µg/l)</th>
<th>Liver (ng/g wet weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>0.2</td>
<td>0.09</td>
<td>16.7</td>
</tr>
<tr>
<td>Adult liver stored</td>
<td>0.7</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Identically PKU on diet</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Normal children</td>
<td>1.78±0.79</td>
<td>2.46±1.76</td>
<td>—</td>
</tr>
<tr>
<td>Normal adults</td>
<td>1.81±0.64</td>
<td>2±1.32</td>
<td>—</td>
</tr>
<tr>
<td>Adults at abdominal operation</td>
<td>—</td>
<td>—</td>
<td>375±232</td>
</tr>
</tbody>
</table>

The levels of total biopterin activity in liver are markedly reduced, as are the levels in serum and urine. These results suggest that the patient, like that of Rey et al. (1977) and another reported recently by Kaufman et al. (1978), is deficient in biopterin. It remains to be explained why other measurements of hepatic cofactor activity failed to demonstrate an abnormality in Dr Bartholomé’s case (Kaufman et al., 1975; Bartholomé et al., 1977).

Mr Leeming thanks Dr Bartholomé for allowing investigation of the patient.

References


Dr Schaub and co-authors comment:
In our Short Report (Archives, 1978, 53, 674), it was not our intention to claim the first description of a defect of biopterin synthesis. We only wanted to show that tetrahydrobiopterin (BH₄) can be absorbed from the gut and be applied to lower the blood phenylalanine level in atypical PKU due to a suspected defect of biopterin synthesis.

Nevertheless, in the meantime we have been able to localise the metabolic block in our patient (Niederwieser et al., 1979). Using high-voltage paper electrophoresis we found large amounts of neopterin in urine but no trace of biopterin or L-erythro-7, 8-dihydrobiopterin (BH₄). A comparable decrease of serum phenylalanine was observed after an oral administration of either BH₄, BH₃, or L-sepiapterin (Curtius et al., 1979). The last is postulated to be an intermediate in the biosynthesis (Eto et al., 1976; Gal et al., 1978) of BH₃ from D-erythro-7, 8-dihydrobiopterin triphosphate (NH₄-P₃). Therefore, the metabolic block in this child must be between NH₄-P₃ and L-sepiapterin (Figure).

Dr Schaub and co-authors comment:
In our Short Report (Archives, 1978, 53, 674), it was not our intention to claim the first description of a defect of biopterin synthesis. We only wanted to show that tetrahydrobiopterin (BH₄) can be absorbed from the gut and can be applied to lower the blood phenylalanine level in atypical PKU due to a suspected defect of biopterin synthesis.

Nevertheless, in the meantime we have been able to localise the metabolic block in our patient (Niederwieser et al., 1979). Using high-voltage paper electrophoresis we found large amounts of neopterin in urine but no trace of biopterin or L-erythro-7, 8-dihydrobiopterin (BH₄). A comparable decrease of serum phenylalanine was observed after an oral administration of either BH₄, BH₃, or L-sepiapterin (Curtius et al., 1979). The last is postulated to be an intermediate in the biosynthesis (Eto et al., 1976; Gal et al., 1978) of BH₃ from D-erythro-7, 8-dihydrobiopterin triphosphate (NH₄-P₃). Therefore, the metabolic block in this child must be between NH₄-P₃ and L-sepiapterin (Figure).

Figure Biopterin biosynthesis from guanosine triphosphate and location of the dihydrobiopterin synthetase defect.

References


JÜRGEN SCABA
Children's Hospital, University of Munich, Lindwurmstrasse 4, D-8 München 2, Western Germany
A. NIEDERWIESER AND H. CH. CURTIUS
Department of Pediatrics, University of Zurich, Switzerland