Fig. 3.—Patient after surgical repair.

were replaced within the spinal canal. The meninges were repaired and the bony defect covered by two layers of lumbar fascia.

There was some superficial wound infection, as there had been after the first operation, but healing was complete after 17 days (Fig. 3). No change in the neurological state of the legs occurred but it was noticed that the child was passing urine very frequently and was constantly wet.

Follow-up. At the age of 9 months, the child was alert and progressing normally. Her head circumference was 43 cm and there was no evidence of hydrocephalus. The neurological function of the legs had returned to normal, and the mother declared that she was no longer wet and had normal sphincter function.

Discussion

The presence of two distinct spinal meningoceles is very unusual. Potter (1962) says that she has observed 2 cases in the dorsal and lumbar regions, in one of which there was an associated hydrocephalus and Arnold-Chiari malformation. Bertan and Wilson (1968) described a case of combined thoracic and lumbosacral myelomeningocele. This child also developed hydrocephalus after successful excision of both sacs and succumbed to septicaemia after the insertion of a ventriculoatrial shunt.

Occipital meningoceles are often associated with spina bifida of the upper cervical segments, and in severe cases may constitute an encephalomyelocoele. In such cases, however, there is no segment of normal spine in between the occipital and the spinal defects.

Fahrenkrug and Hoigaard (1963) described the radiological findings in multiple paravertebral lumbar meningoceles, but their patient was not operated upon.

Meningoceles have been described with other congenital anomalies of the vertebral column, while hydrocephalus and the Arnold-Chiari malformation are common associations. Von Recklinghausen’s disease is frequently found with intrathoracic meningoceles, but its rare coexistence with lumbosacral meningoceles and meningomyeloceles is regarded as no more than coincidental (Levene, 1959).

Summary

A child with both a thoracic meningocele and a lumbar meningomyelocele is described. Both lesions were successfully operated upon; hydrocephalus did not develop and there was no obvious neurological defect.

I acknowledge, with thanks, the permission of the Chief Medical Officer, Ministry of Health, Uganda, to publish this paper.

REFERENCES


IAN C. BAILEY

The Neurosurgical Unit, Mulago Hospital, Kampala, Uganda, East Africa.

Classical and Mild Phenylketonuria in a Family

A few patients with untreated phenylketonuria (PKU) escape the severe mental retardation usual in the untreated disease. Some of these patients have classical PKU but most have a related condition which has been called mild PKU or hyperphenylalaninaemia. Hsia, O’Flynn, and Berman (1968) reviewed 43 untreated phenylketonurics who were ‘atypical’ in that the IQ was 70 or higher. Of these patients, 18 had plasma phenylalanine levels of 21 mg/100 ml or more and were regarded as having classical PKU, while 19 had plasma phenylalanine levels of 20 mg/100 ml or less and were regarded as having hyperphenylalaninaemia; in 6 cases the plasma phenylalanine level was not known.

We describe here a family of 5 children, 4 of whom have PKU. The youngest child has classical PKU diagnosed in the neonatal period and is on a low phenylalanine diet. 3 of her 4 older sibs have untreated mild PKU each with a blood
phenylalanine level of 20 mg/100 ml while on an ordinary diet. The eldest of these 3 sibs has normal intelligence while the other 2 are only moderately retarded.

**Case Report**

The 5th child (J.B.) of healthy parents, birthweight 2.96 kg, was born in December 1966. She was fed on National Dried Milk and on the 7th day routine Guthrie testing showed a blood phenylalanine level of 30 mg/100 ml. At 14 days the serum phenylalanine was 25 mg/100 ml and the serum tyrosine 3.5 mg/100 ml. Despite the raised blood phenylalanine level, the urine was negative for phenylpyruvic acid. Because of the high blood phenylalanine level, a low phenylalanine diet was started at 16 days. After 2 days on this diet the blood phenylalanine level had fallen to less than 2 mg/100 ml. Subsequent adjustment of the phenylalanine content of the diet led to satisfactory control. At 2 months a trial of a normal diet using dried milk feeds caused a rise in the blood phenylalanine to 30 mg/100 ml, though the urine remained persistently negative for phenylpyruvic acid. A low phenylalanine diet was restarted after this trial. At 1 year a further trial of a diet with a normal phenylalanine content was instituted using Complan to supply 40 g protein, as suggested by Stephenson and McBean (1967). On this diet the blood phenylalanine again rose to 30 mg/100 ml and for the first time her urine was positive for phenylpyruvic acid; the urine also contained orthohydroxyphenylacetic acid. As these findings confirmed the diagnosis of classical phenylketonuria a low phenylalanine diet was restarted and has been continued since. At 13 months her developmental quotient was 103 (Griffiths scale) and at 30 months was 97 (Terman Merrill scale).

Her 4 sibs, none of whom had previously been screened for PKU, were investigated, and the results (Table) indicate that 3 of them (J.B., A.B., and I.B.) have mild phenylketonuria. The di-tary history of these children was normal, except that J.B. was reluctant to take mixed feeding and was on bottle feeds of dried milk until more than 1 year old.

J.B., whose IQ is 104, is making average progress at secondary school. The psychologist commented that he is very tense and anxious and defends against this by clowning, pressure of talk, and a rather uninhibited call for reassurance. A.B., whose IQ is 70, and I.B., whose IQ is 63, attend a primary school but are said to be slower at learning than their older sibs. I.B. was 4 years old when PKU was diagnosed, and in view of her low IQ an attempt was made to give her a low phenylalanine diet. However, her mother found it impossible to keep her to the diet and the attempt was abandoned. The unaffected sib, M.B., has an IQ of 100 and is at a secondary school.

The parents were investigated for PKU with normal results (Table).

**Discussion**

In classical PKU the blood phenylalanine level rises rapidly in the first week or two of life to levels which are normally above 30 mg/100 ml, phenylpyruvic acid and its catabolites are excreted in the urine, and in the absence of dietary therapy mental retardation usually develops (Carpenter, Auerbach, and DiGeorge, 1968). A complete absence of phenylalanine hydroxylase activity in the liver has been demonstrated in this condition (Justice, O'Flynn, and Hsia, 1967).

In mild PKU the blood phenylalanine is only slightly or moderately raised to no more than 20 mg/100 ml, and phenylpyruvic acid may or may not be excreted in the urine. In the absence of dietary therapy, patients with mild PKU do not show the severe mental retardation associated with untreated classical PKU; they may be moderately retarded or even have normal intelligence (Berman et al., 1969).

**TABLE**

**Biochemical Findings and Intelligence Quotients (Terman Merrill) of Relatives of E.B.**

<table>
<thead>
<tr>
<th>Relative</th>
<th>Date of Birth</th>
<th>IQ (Estimated Feb. 1968)</th>
<th>Blood Phenylalanine (mg/100 ml)</th>
<th>Urinary Phenylpyruvic Acid (Jan. 1968)</th>
<th>Urinary O-Hydroxyphenylacetic Acid (mg/g creatinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father</td>
<td>Adult</td>
<td>Not tested</td>
<td>Jan. 1968: &lt;2</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Mother</td>
<td>Adult</td>
<td>Not tested</td>
<td>Jan. 1970: &lt;2</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>J.B. Male</td>
<td>27.3.56</td>
<td>104</td>
<td>20</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>M.B. Female</td>
<td>19.4.58</td>
<td>100</td>
<td>20</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>A.B. Female</td>
<td>26.11.59</td>
<td>70</td>
<td>20</td>
<td>Positive</td>
<td>Trace</td>
</tr>
<tr>
<td>I.B. Female</td>
<td>10.7.63</td>
<td>63</td>
<td>20</td>
<td>Positive</td>
<td>Trace</td>
</tr>
</tbody>
</table>

*One-dimensional paper chromatography (semi-quantitative) for O-Hydroxyphenylacetic acid (Jan. 1968).
would tend to skew the results of well-controlled dietary therapy in favour of normal mental development and function. Despite these criticisms of past studies, the efficacy of dietary therapy in classical PKU is generally conceded and further controlled trials are unlikely to be ethically acceptable.

Most patients with mild PKU have been diagnosed in the newborn period as a result of mass screening by the Guthrie test. While some of these patients have been treated from early infancy with a low phenylalanine diet, the relatively good prognosis for intellectual attainment in untreated mild PKU raises serious doubts about the need for an expensive and unpalatable low phenylalanine diet. One of the untreated children in the family we describe whose blood phenylalanine was 20 mg/100 ml while on an ordinary diet had an IQ of 104. Further evidence that dietary therapy is probably not necessary in mild PKU is provided by Berman et al. (1969) who reviewed all cases with persistent blood phenylalanine levels of 6 mg/100 ml or higher, with normal blood tyrosine levels, seen during a three-year period in 11 centres in the U.S.A. They arbitrarily divided these patients into group 1 patients with maximum blood phenylalanine levels of 20 mg/100 ml or higher, and group 2 patients with maximum blood phenylalanine levels below 20 mg/100 ml. Group 1 patients had classical PKU, group 2 patients who were regarded as having hyperphenylalaninaemia showed normal mental development whether or not a low phenylalanine diet had been given.

If it is assumed that the lower the IQ the more severe the disease, then it appears that in the family we have described the severity of the mild PKU increases with each successive birth of an affected child, as the IQ of the eldest affected child is 104, of the next 70, and of the next 63. The birth of the fifth child with classical PKU might be regarded as yet a further stage in the increasing severity of the disease.

Summary

A positive Guthrie test in the newborn period led to the diagnosis of classical phenylketonuria in a female infant. 3 of her 4 sibs proved to have mild phenylketonuria which was previously unsuspected. The eldest of these affected sibs has normal intelligence, and the other 2 have IQs of 70 and 63.

We are grateful to Dr. M. S. McBean for her valuable help in the investigation of this family; also to Dr. J. S. Stevenson and his department who carried out the Guthrie tests.

References


N. A. Coutts* and W. M. Fyfe Paediatric Unit, Stobhill General Hospital, Glasgow N.

*Correspondence to: Dr. N. A. Coutts, Hawkhead Hospital, Hawkhead Road, Paisley, Renfrewshire.

Treatment of Letterer-Siwe Disease

The prognosis in untreated Letterer-Siwe disease is extremely poor; Lahey (1962) found no survivors among 27 infants with the disease who received no treatment. Even with treatment, the majority of those infants who are affected in the first year of life eventually die (Lahey, 1962). Occasional long-term survivors have been reported after no therapy, or after treatment with antibiotics (Berman, 1966). Apparent cures after steroid or antimetabolite drug therapy have been reported. The antimetabolite drugs used include vinblastine sulphate (Beier, Thatcher, and Lahey, 1963), vincristine sulphate (Hertz and Hambrick, 1968), aminopterine (Freud, 1961), and daunomycin (Segni, Mastrandelo, and Tortorolo, 1968). Cyclophosphamide has also been used with success in some instances (Esterly and Swick, 1969), but in other patients no response was seen.

Case Report

The second child of unrelated parents weighed 3·35 kg at term after a normal pregnancy. At 10 weeks he developed a scaly, erythematous rash on his chest which spread to his limbs. At first this responded to topical steroids but then recurred. At 14 weeks he began to cough and to vomit after meals. He became increasingly breathless and lost 0·57 kg in weight in 7 days.