necessary to keep the boy isolated to protect him from infections. The period of isolation was prolonged because of the varicella and the upper respiratory infection. There were remarkable fluctuations of the immunoglobulin values from time to time, probably partly due to the infections. We consider these immunoglobulin reactions as a sign of normal capability of immunoglobulin production. This case thus showed the development of immunoglobulins by the infant itself, uninfluenced by passively transferred maternal immunoglobulins.

Summary

The immunoglobulin production in a normal boy born of a severely hypo-γ-globulinaemic mother was followed during the first 6 months of life. As the mother did not receive γ-globulin treatment during pregnancy, the development of immunoglobulins by the infant was uninfluenced by passively transferred maternal immunoglobulins. In the cord blood there was >1 mg/100 ml each of IgA, IgG, and IgM. A spontaneous increase in the immunoglobulins was observed during the first month and continued during the following months.

REFERENCES


H. BAEGGAARD LAURSEN* and M. FYORD CHRISTENSEN
University Clinic of Paediatrics, Århus Kommune-
hospital, Denmark.

*Correspondence to Dr. H. Baeggaard Laursen.

Dietary requirement of phenylalanine in infants with hyperphenylalaninaemia

Hyperphenylalaninaemia has been variously defined and named (Carpenter, Auerbach, and DiGeorge, 1968; Jervis, 1967; Scriver, 1967). We define it as the condition in which plasma phenylalanine is above 5 mg/100 ml but usually below 20 mg/100 ml on a normal diet. Originally we, like many others, treated children with this condition, but now they are maintained on a normal diet and brain damage is not evident. Our belief in the safety of not treating these children has been strengthened by the discovery of a family containing 3 hyperphenylalaninaemic children when the youngest was detected by routine Guthrie tests. The two older sibs had phenylalanine levels consistently between 10 and 20 mg/100 ml and were mentally normal.

In 1967, Hsia and O'Flynn stated that the phenylalanine intake tolerated by hyperphenyl-
alanaemic individuals (90–100 mg/kg per day) was higher than that of classical phenylketonuria (30–40 mg/kg per day). This suggests that dietary management of these individuals could be much less restrictive, and therefore a low phenylalanine diet would be worth while, even though the risk of brain damage in this condition appears minimal. The purpose of this study was to see if hyperphenyl-
alanaemic children could have their plasma phenylalanine levels maintained at a desirable level on a less restricted diet than classical phenylketonuric patients.

Patients and treatment

Four hyperphenylalaninaemic children were initially treated with low phenylalanine diets until the age of 9 months with the aim of keeping their serum phenylalanine levels below 10 mg/100 ml. These children were all detected by routine Guthrie test (Guthrie and Susi, 1963) in the 6 years before June 1969. In the same period 5 children with classical phenylketonuria were similarly detected and were randomly assigned to a treatment group in which the aim was to keep the plasma phenylalanine level below 5-5 and 10 mg/100 ml. Accurate dietary records of these children were kept and their plasma phenylalanine levels were measured at roughly weekly intervals. Plasma phenylalanine was measured by the fluorometric method of McCaman and Robins (1962) as modified by Wong, O'Flynn, and Inouye (1964).

All the children designated phenylketonuric had phenylalanine loads performed in the first year of life which confirmed the diagnosis of classical phenylketo-
nuria. The 4 children with hyperphenylalaninaemia are now off diet with raised plasma phenylalanine levels and normal intelligence.

Results

The Table shows the plasma phenylalanine level and phenylalanine intake (expressed as mg/kg body weight per day) of the 4 hyperphenylalaninaemic
Short reports

Phenylalanine intake in mg/kg per day in infants with hyperphenylalaninaemia

<table>
<thead>
<tr>
<th>Age (mth)</th>
<th>4 hyperphenylalaninaemic patients</th>
<th>5 phenylketonuric patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intake* (mg/kg per day)</td>
<td>Plasma level* (mg/100 ml)</td>
</tr>
<tr>
<td>3</td>
<td>38±12</td>
<td>8.5±5.2</td>
</tr>
<tr>
<td>4</td>
<td>57±19</td>
<td>10.0±5.8</td>
</tr>
<tr>
<td>5</td>
<td>50±14</td>
<td>9.8±5.5</td>
</tr>
<tr>
<td>6</td>
<td>36±6</td>
<td>4.7±2.3</td>
</tr>
<tr>
<td>7</td>
<td>32±9</td>
<td>8.3±2.1</td>
</tr>
<tr>
<td>8</td>
<td>29±1</td>
<td>6.2±1.3</td>
</tr>
<tr>
<td>Mean</td>
<td>40.3</td>
<td>7.9</td>
</tr>
</tbody>
</table>

*Mean ± 1 SD.

Discussion

The results shown above do not bear out the suggestion that children with hyperphenylalaninaemia tolerate more phenylalanine in their diet than classical phenylketonurics if one attempts to keep their plasma phenylalanine below 10 mg/100 ml. This is in contradistinction to their behaviour when not on any diet, when the hyperphenylalaninaemic individual usually has a plasma phenylalanine level below 20 mg/100 ml, while the level in classical phenylketonuria is usually much greater than 20 mg/100 ml.

It should be emphasized that all the patients in this study have had repeat loading studies with phenylalanine which have confirmed the diagnosis of classical phenylketonuria in those so designated, while all 4 hyperphenylalaninaemic individuals are now on normal diets with plasma phenylalanine levels usually below 20 mg/100 ml. Thus, there is little doubt that their diagnoses are correct by accepted criteria.

It is of interest that the dietary methods used to keep the plasma phenylalanine level below 10 mg/100 ml should have resulted in an almost identical intake of phenylalanine, on a body weight basis, in both groups. This is at variance with the view expressed by Hsia and O’Flynn in 1967. They do not supply any data to support the view that children with hyperphenylalaninaemia can tolerate 90 to 100 mg/kg per day of phenylalanine in the diet, nor does a search of the literature reveal such data. Thus, it is impossible to comment further on the disparity between our findings and their statement.

Although this study does not shed any light on the cause of hyperphenylalaninaemia, it does suggest that the patient is not able to handle a reduced intake of phenylalanine any more effectively than patients with phenylketonuria, whereas he obviously tolerates a normal intake of phenylalanine much better than those with classical phenylketonuria.

It also suggests that dietary restriction in infants with hyperphenylalaninaemia will be as severe as in classical phenylketonuria. Because the danger of brain damage in hyperphenylalaninaemia appears remote, such dietary restriction does not appear justified.

Summary

This study was undertaken to ascertain whether hyperphenylalaninaemic children could have their plasma phenylalanine levels reduced to desirable levels by a diet less restrictive than that used in classical phenylketonuria. 4 hyperphenylalaninaemic children were treated with low phenylalanine diets until the age of 9 months with the aim of keeping their plasma phenylalanine below 10 mg/100 ml. They were compared with 5 children with classical phenylketonuria in which the aim was to keep plasma phenylalanine between 5.5 and 10 mg/100 ml.

The average phenylalanine intakes for both groups were almost identical (hyperphenylalaninaemia 40.3 mg/kg per day, phenylketonuria 39.8
mg/kg per day). This suggests that dietary restriction in infants with hyperphenylalaninaemia will be as severe as in classical phenylketonuria.

This work was partially supported by USPHS grants HD00341 and HD00131. D.R.L. was the recipient of a U.S. Post-doctorate NIH Fellowship F05 TW 1046 while undertaking this study. The authors thank Robert Colwell for plasma phenylalanine measurements.

**References**


D. R. LINES* and MARILYN SWANSON

Joseph P. Kennedy Jr. Laboratories, University of Wisconsin, Madison, Wisconsin, U.S.A.

*Correspondence to Dr. D. R. Lines, Department of Paediatrics, University of Adelaide, Adelaide Children’s Hospital, North Adelaide, South Australia.

**Red cell phospholipid determination in diagnosis of neurological disease**

In many cases of disorders of the central nervous system in childhood there is associated mental subnormality. Frequently the severity of the physical disorder makes the assessment of the degree of intellectual deficit a very difficult problem, especially when blindness is a contributory factor. The aetiology of such cases is extremely variable, but from the point of view of prognosis and family counselling the differentiation between disorders due to prenatal, perinatal, or postnatal brain damage and a demyelinating or dysmyelinating disease is most important. Clearly, any simple procedure enabling such a differentiation in order to select suitable cases for more sophisticated procedures, such as cerebral biopsy, would prove invaluable.

Following the report by Hooghwinkel, van Gelderen, and Staal (1969) that the sphingomyelin content of erythrocytes was found to be low in children with progressive brain disease, we decided to apply their method, modified in the light of more recent technical developments, to a number of patients suffering from severe mental and physical handicaps of uncertain cause. In all, 21 children were examined, both male and female, in the 3 to 14 years age group. In addition, 4 other groups of children with previously diagnosed brain disorders were studied (37 cases), along with a group of normal subjects (25 cases). The classification of the 37 cases broadly follows that of Hooghwinkel et al. (1969) except that we had no patients in his Group II (juvenile amaurotic idiocy), but we had an additional group (Ia) consisting of patients not expected to show abnormal erythrocyte sphingomyelin content.

**Patients**

There were 83 patients studied, and they were divided into groups as follows.

**Group I.** Normal subjects. These were 25 subjects who were either inpatients of Lea Castle Hospital, Kidderminster, or were attending outpatient departments of Birmingham Children’s Hospital or the Royal Orthopaedic Hospital, Birmingham. These patients were selected because diagnosis and treatment were considered unlikely to affect the quality of the erythrocyte membrane, and it was possible to use the red cell mass from a heparinized specimen already obtained for the determination of some substance in the plasma. 12 males and 13 females were included, their ages ranging from 2 months to 16 years.

**Group I(a).** Children with known causes of brain damage not expected to involve phospholipid metabolism (11 cases). This was a heterogeneous group including meningomyelocele with hydrocephalus 2, Sjögren-Larson syndrome 1, congenital hydrocephalus 1, Duchenne-type muscular dystrophy 1, Sturge-Weber syndrome 1, tuberous sclerosis 2, chromosomal disorders 2, and striatopallidal degeneration 1.

**Group II.** Juvenile amaurotic idiocy. (There were no cases in the present study.)

**Group III.** Cases of proven mucopolysaccharidosis (2 cases).

**Group IV.** Cases of proven leucodystrophy (3 cases).

**Group V.** Cases of dementia or amnesia of unknown origin (21 cases), including (a) familial cases 4, (b) cases with progressive degeneration of unknown cause 3, (c) amnesia with epilepsy 3, (d) amnesia with spasticity 7, (e) severe amnesia alone 4.