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soun for the ammonia assay; and Dr. J. Dochain for giving us the opportunity to examine this patient.

REFERENCES


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Decreased antihaemophilic globulin and leucocyte response to epinephrine in preterm infants

The ability of the reticuloendothelial system (RES) and the spleen to respond quickly and efficiently to challenge is thought to be an important factor in the prevention of acute fulminating infections. The increased susceptibility of preterm infants to infections cannot be explained by the deficiencies in their immune system, and the importance of the RES has therefore recently received attention (Gotoff, 1974). Measurement of RES and splenic activity is difficult, especially in preterm neonates, and the idea of splenic hypofunction in preterm infants comes from indirect evidence. Holroyde, Oski, and Gardner (1969) observed a high percentage of 'pocked' erythrocytes in the blood of preterm infants, similar to those seen in patients after splenectomy, which they thought was due to the immaturity of the RES, mainly of the spleen. Others (Casper, Rodely, and Thatcher, 1974) noted their presence in patients with a nonfunctional spleen. Acevedo and Maurer (1963) showed that preterm newborns do not remove erythrocytes containing Heinz bodies as efficiently as normal babies, therein resembling splenectomized individuals.

Epinephrine injections (or infusions) have well-known, if not well-understood, effects upon the RES and the spleen, and two of them are easily investigated. They are (1) the rise in the number of formed elements such as leucocytes in the circulating blood (Chatterjea, Dameshek, and Stefanini, 1953), and (2) the rise in the level of plasma antihaemophilic activity (Ingram, 1961). Information about these effects of epinephrine in neonates is lacking, so we investigated them.

Subjects and methods

Two groups of neonates (groups 1 and 2) between the ages of 2 and 4 days and two groups of older children (groups 3 and 4) were studied.

Group 1. Comprised 21 preterm infants (15 males, 6 females) with a gestational age of about 30–38 weeks and a birthweight of 1100–2400 g.

Group 2. Comprised 23 term infants (12 males, 11 females) whose birthweight was between 2900 and 3440 g.

Group 3. Comprised 20 children aged 3 months to 6 years (10 males and 10 females) who served as a control group. All were apparently healthy and had no haematological disorder.

Group 4. Comprised 13 children who had had splenectomy (12 because of trauma, 1 for spherocytosis) and 1 with congenital asplenia syndrome.

With written parental permission, blood was drawn from a vein before and 30 minutes after a subcutaneous injection of epinephrine 0·01 mg/kg. A leucocyte count was made simultaneously, on capillary blood. The antihaemophilic activity of the plasma was estimated by the one-stage PTT test (Rodman, Barrow, and Graham, 1958), using a commercial antihaemophilic globulin-deficient serum (Dade Laboratory).

Results

Tables I and II summarize our findings. Before the injection there was not much difference between the four groups either in antihaemophilic activity or leucocyte count. But the differences in the response to epinephrine were highly significant. While the term infants reacted similarly to the controls the response of the preterm neonates was negligible, as was that of the splenectomized group. No differences were observed between males and females in any of the four groups.

Discussion

Our data suggest that preterm neonates fail to react normally to epinephrine injections, so far as
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**TABLE I**

*Mean (± SEM) changes in antihaemophilic globulin (Factor VIII) activity after epinephrine injection*

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of tests</th>
<th>Before injection</th>
<th>After injection</th>
<th>% rise</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (± SEM)</td>
<td>Mean (± SEM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range</td>
<td>Range</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>21</td>
<td>146.2 ± 23.2</td>
<td>168.2 ± 37.8</td>
<td>25.09 ± 18.3</td>
<td>NS</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>133.8 ± 16.9</td>
<td>139.4 ± 48.9</td>
<td>15.46 ± 30.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>230.8 ± 24.1</td>
<td>426.5 ± 38.0</td>
<td>102.75 ± 18.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>135 ± 14.2</td>
<td>152.7 ± 30.6</td>
<td>18.20 ± 16.32</td>
<td>NS</td>
</tr>
</tbody>
</table>


**TABLE II**

*Mean (± SEM) changes in leucocyte count after epinephrine injection*

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of tests</th>
<th>Leucocytes (per mm³)</th>
<th>% rise</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before injection</td>
<td>After injection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean (± SEM)</td>
<td>Mean (± SEM)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range</td>
<td>Range</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>21</td>
<td>11768 ± 1261</td>
<td>117 007 ± 1146</td>
<td>1.64 ± 4.25</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>8842 ± 1122</td>
<td>15 077 ± 1679</td>
<td>74.46 ± 7.86</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>8520 ± 693</td>
<td>14 430 ± 972</td>
<td>80.21 ± 9.05</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>10 800 ± 1200</td>
<td>11 000 ± 1120</td>
<td>0.01</td>
</tr>
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</table>


antihaemophilic activity and leucocyte responses are concerned. This might be due to the immaturity of their RES and, perhaps primarily, of their spleen. These results are consistent with the findings of Holroyde *et al.* (1969), using the percentage count of 'pocked' erythrocytes as an index of RES immaturity. Falter *et al.* (1972) found a lack of normal response to epinephrine infusions in patients with sickle-cell anaemia correlated well with their splenic activity as measured by 99Tc uptake. Webster *et al.* (1967) showed that in dogs antihuman globulin is normally secreted by the spleen, and Rizza and Eipe (1971) showed that it can be produced and stored in other RES tissues.

Perhaps in older people the RES can compensate more quickly and efficiently for an absent or non-functioning spleen than it can in early infancy. The inability to react to epinephrine might reflect an inefficiency, due to immaturity of the RES, in reacting to other challenges such as acute infections. One aspect of this lack of reaction may be the absence of leucocytosis often found in infections in preterm neonates, which would help to explain the high susceptibility of these patients to fulminating infections.

**Summary**

Twenty-one preterm and 23 term neonates, 13 splenectomized children and one with congenital asplenia, and 20 normal children were examined for plasma antihaemophilic activity and for blood leucocyte levels before and 30 minutes after a subcutaneous injection of epinephrine 0.01 mg/kg. The basal values for antihaemophilic activity were similar for the 4 groups. The response to epinephrine was a trivial rise in antihaemophilic activity in the preterm group, while the rise in the term newborns was comparable to that of the normal children. The asplenic children all showed a trivial rise. The leucocyte response was also negligible in both the preterm neonates and asplenic groups, while in the term infants it was comparable to that seen in the normal children. These results may indicate an incapacity of the preterm newborn infant's reticuloendothelial system and spleen to react to other challenges, such as bacterial infection.

**References**


Jaundice and bilirubin levels in Greek children with favism

Favism is common in certain Mediterranean countries, especially Greece, Italy, Israel (among Sephardic Jews), and China. It affects individuals deficient in red cell glucose 6-phosphate dehydrogenase (G-6-PD) and mainly those with the Mediterranean variant. The main clinical features are severe anaemia, haemoglobinuria, and jaundice (Harris, 1963; Dacie, 1967) of these, only anaemia; has been studied (Kattamis, Kyriazakou, and Chaidas, 1969). The severity of jaundice and the bilirubin levels during the acute favic crisis have not been studied, though bilirubin levels were occasionally measured in individual cases by Sansone, Piga, and Segni (1958). During the past decade we have noticed in a large series of patients with favism that jaundice was not present in all cases and that when present its severity varied considerably. We therefore noted the incidence of jaundice in a series of 85 patients with favism and measured its severity by estimating bilirubin levels during the acute haemolytic crisis.

Patients

Eighty-five patients with favism aged from 1·5 to 12 years admitted to the 1st Department of Paediatrics of the University of Athens from 1969 to 1972 were studied. Favism was diagnosed when an acute haemolytic syndrome occurred after the ingestion of fresh or dry fava beans. The clinical signs consisted of gross haemoglobinuria and anaemia, while the laboratory findings were of fragmented red cells, spherocytosis, low haemoglobin, and reticulocytosis associated with red cell G-6-PD deficiency.

On admission the patients were carefully examined for clinical jaundice, and laboratory investigations before transfusion included Hb, packed cell volume, red cell and reticulocyte counts, and bilirubin determination; G-6-PD activity was measured by the Brilliant Cresyl Blue (BCB) decolorization test. In girls in addition to the BCB test enzymic activity was determined quantitatively and histochemically by the cyanmethaemoglobin elution technique. The results were measured according to standards used in our laboratory (Kattamis, 1967).

Results

The total bilirubin levels in 85 children during the acute favic crisis and before transfusion are shown in Fig. 1. The severity of jaundice was related to the bilirubin level.

The bilirubin levels varied widely, ranging from 0·5 mg/100 ml to 13 mg/100 ml with a mean (±SD) of 3·54±2·67 mg/100 ml. Low bilirubin levels (2 mg/100 ml) were found in 34 (40%) of the patients. At these levels jaundice was usually clinically undetectable. Notably 17 (20%) had normal bilirubin levels (<1 mg/100 ml) despite acute haemolysis and anaemia. In the remainder the variations in bilirubin levels and jaundice were as follows: 31 (38%) had mild jaundice with bilirubin levels ranging from 2·0 to 4·9 mg/100 ml; 16 (19%) had moderate jaundice with bilirubin levels of 5·0 to 7·9 mg/100 ml; and only 3 (4%) had severe jaundice with bilirubin exceeding 8 mg/100 ml.

As a rule bilirubin was unconjugated though a small