Levels of albumin, α-fetoprotein, and IgG in human fetal cerebrospinal fluid

The estimation of total protein and the relative concentration of specific components of the cerebrospinal fluid (CSF) have been the subject of many investigations because of their significance as diagnostic aids in various pathological conditions (Kabat, Moore, and Landow, 1942; Burtin, 1960; Laterre, Heremans and Carbonara, 1964; Davson, 1967; Laterre, 1973). Protein levels in samples of lumbar CSF from normal adults range between 20 and 40 mg/100 ml. During the first 3 months of life the total protein concentration of CSF appears to be higher, even reaching 120 mg/100 ml.

We report the results of estimating the levels of three proteins, α-fetoprotein (AFP), albumin, and IgG, in CSF from human fetuses. These studies are relevant to the question of the origin of AFP in amniotic fluids of fetuses with 'open' neural-tube defects and to the problem of the permeability of the blood-brain barrier during fetal life.

Materials and methods

Samples of CSF were obtained by aspiration with a syringe either from the lateral ventricles of the brain or from the upper cervical regions of the spinal cord. Six samples which were absolutely clear and free from contamination by blood were assayed; other samples, slightly contaminated, were discarded. 2 fetuses were fresh specimens, spontaneously aborted and apparently normal. 4 were obtained by hysterotomy; of these, 3 had chromosome abnormalities (Down's syndrome), while the fourth was a male fetus borne by a female carrier of the gene for haemophilia. CSF from these fetuses was collected within 2–5 hours of the hysterotomy. Ages of the fetuses ranged between 16½ and 25½ weeks (Table I).

### Table I

<table>
<thead>
<tr>
<th>Fetus</th>
<th>Age (w)</th>
<th>Causes of abortion</th>
<th>Chromosome complements</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16½</td>
<td>Spontaneous</td>
<td>Not tested</td>
</tr>
<tr>
<td>2</td>
<td>19½</td>
<td>Spontaneous</td>
<td>Not tested</td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>Induced</td>
<td>47,XY, + G</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>Induced</td>
<td>46,XY</td>
</tr>
<tr>
<td>5</td>
<td>25½</td>
<td>Induced</td>
<td>46,XY – G + t(DqGq)</td>
</tr>
<tr>
<td>6</td>
<td>25½</td>
<td>Induced</td>
<td>47,XY, + G</td>
</tr>
</tbody>
</table>

Albumin level was measured by the single radial diffusion technique and AFP by the one dimensional antigen-antibody electrophoresis (rocket technique), as previously described (Seller et al., 1973). IgG levels were estimated using commercially available immunoplates (Behringwerke, AG, Marburg, Germany).

Results and conclusions

AFP levels in fetal CSF were found to decline from 1220 μg/ml in the 16½-week-old fetus to 52 and 60 μg/ml in the older fetuses tested (Table II). Reduction of the concentration of AFP in CSF, in relation to the ages of the fetuses, was more rapid than that of the levels of AFP in fetal sera. The ratios between the amounts of albumin and AFP in CSF increased with age, passing from 1·8 in a fetus 18 weeks old to 20 in a fetus 25½ weeks old.

IgG in adult CSF ranges from 20–40 μg/ml (Davson, 1967; Laterre, 1973). It was therefore of great interest to find higher levels of IgG in the CSF of the fetuses. Since most of the IgG present

### Table II

<table>
<thead>
<tr>
<th>Fetus</th>
<th>Levels of AFP (μg/ml)</th>
<th>CSF levels (μg/ml) of</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1) CSF</td>
<td>(2) Serum</td>
</tr>
<tr>
<td>1</td>
<td>1220</td>
<td>Not tested</td>
</tr>
<tr>
<td>2</td>
<td>1040</td>
<td>Not tested</td>
</tr>
<tr>
<td>3</td>
<td>420</td>
<td>2720</td>
</tr>
<tr>
<td>4</td>
<td>71</td>
<td>1380</td>
</tr>
<tr>
<td>5</td>
<td>52</td>
<td>840</td>
</tr>
<tr>
<td>6</td>
<td>65</td>
<td>690</td>
</tr>
</tbody>
</table>
in fetal sera is derived from the maternal circulation and there is no evidence that these proteins are secreted by the choroidal plexi, it seems that IgG molecules present in fetal CSF are derived from blood. These findings support the suggestion that the permeability of the blood-brain barrier is not fully developed during fetal life (Davson, 1967).

The presence of high AFP levels in fetal CSF raises another important point in relation to the increased levels of this fetal protein in the amniotic fluids of fetuses with ‘open’ neural-tube defects (Brock and Sutcliffe, 1972; Seller et al., 1973). It has been repeatedly suggested that in conditions where the neural tissue is exposed, AFP passes from the CSF into the amniotic cavity. The observation that AFP is present in high concentration in fetal CSF seems to support this hypothesis, though other mechanisms may be involved as well (Adinolfi, 1974).

Summary
Cerebrospinal fluid from 6 fetuses, 16½–25½ weeks of gestation, was assayed for the levels of α-fetoprotein, albumin, and IgG. All these proteins were present in significant amounts. The level of α-fetoprotein decreased, albumin increased, and IgG remained roughly constant during this period. These results suggest that the permeability of the blood-brain barrier is not fully developed in the fetus.

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References


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Children with duodenal ulcers and their families

Duodenal ulcer in children has been reported with increasing frequency in recent years (Robb, Orszulok, and Odlind-Sme, 1972), but there is little information available concerning the incidence of peptic ulcer in the families of these patients with duodenal ulcer. An effort has been made in this study to determine the incidence of peptic ulcer in the relatives of affected children.

Materials and methods
Thirty-seven children were admitted with duodenal ulcer to this hospital in Dublin from 1960 to 1973. There were 24 boys and 13 girls, ages ranging from 15 months to 14 years. Diagnosis was made by barium meal examination in 34 patients, at operation in 2, and the ulcer was discovered at necropsy in one patient. A family history of peptic ulcer was recorded and was regarded as positive if one or other parent, grandparent, sib, aunt, or uncle was known to have the ulcer on the basis of barium meal examination or previous gastric surgery.

Results
The study revealed that 23 of the 37 children (62%) had a positive family history of peptic ulcer; 8 patients had a negative family history; and in 6 cases no family history could be obtained. A total of 40 relatives were found to have definite ulcers (Table). 13 children had only one relative with an ulcer. In the remaining 10 children there were 2 or more affected relatives.

Investigation of the degree of relationship of affected family members revealed that the most frequently affected relatives were those who had the closest relationship with the children with duodenal ulcers. 19 of 23 children had one or other parents or sib affected with the disease. In 13 children there was a history of peptic ulcer in the father.

Discussion
Our findings show a significant familial aggregation of peptic ulcers and emphasize the importance...
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