Cerebrospinal Fluid Dynamics in the Arnold-Chiari Malformation*

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A myelomenigocele associated with the Arnold-Chiari malformation is now one of the commonest neonatal surgical emergencies. Hydrocephalus used to be the main cause of death in these infants during the first year of life, but since the advent of ventriculo-atrial shunting procedures the mortality and morbidity have improved. However, the management of the hydrocephalus still remains a serious problem.

In the past, assessment of the hydrocephalus has depended upon the correlation of the clinical signs such as skull size, separation of the sutures, tension of the anterior fontanelle with the CSF pressure, dye studies, and air ventriculography. More recently radio-isotopes have been used to study the production, circulation, and absorption of the CSF. The aim of the present investigation was to measure the movement of CSF before and after ventriculo-atrial shunts in infants with the Arnold-Chiari malformation.

Material and Method

On the evening before the test each patient was given 0.2 ml. of Lugol's iodine by mouth to protect the thyroid gland against any uptake of 131I.

2 μc of radio-iodinated human serum albumin (RISA 131I) in 1 ml 0.9% saline were injected into one lateral ventricle, either by ventricular puncture through the lateral corner of the anterior fontanelle or through a ventriculostomy reservoir (Rickham, 1964, Fig. 1). Approximately 1 ml. samples of CSF from the same ventricle were taken at 1, 4, and 24 hours and placed in previously weighed tubes and sealed. The samples were weighed to determine the volume of CSF. The activity in each sample was counted in a Packard Auto γ Spectrometer well-counter, using a thallium-activated sodium iodide crystal. Total counts of over 10,000 were recorded for each sample and after correction for background activity and isotopic decay the activity was expressed in c.p.m./ml.

Calculation of results. Assuming that uniform mixing of the RISA in the lateral and third ventricles had occurred by the end of 1 hour the volume (V) can be calculated by the comparison of the activity in the 1-hour sample with that of a known standard.

The disappearance of RISA from the lateral ventricle was calculated from the activity remaining in the 4-hour and 24-hour samples of CSF, and expressed as percentages of the 1-hour sample. On plotting these percentages against time on semi-logarithmic paper a straight line is obtained (Fig. 2 and 6). The half-life in hours (T½) was determined by inspection. There was little difference between the slope of the line before and after a ventriculo-atrial shunt, especially when the ventricles were grossly dilated (Fig. 2), and this did not correlate with the clinical findings. One of the reasons for this anomaly was the wide variation found in the size of the ventricular system between different patients, and also in

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Fig. 2.—A. Rate of disappearance of radio-activity in ventricular fluid after injection of RISA showing little difference in the disappearance of RISA before and after a ventriculo-atrial shunt. B. After determining the $T_{1/2}$ and plotting these values on the same scale the difference is more marked and agrees with the clinical findings.

the same patient at different times, due to progressive hydrocephalus.

Assuming a single compartment system at a constant pressure, the rate of flow from the system is related to the volume by the formula:

$$F = \frac{0.693}{T_1} V$$

(Weall and Vetter, 1958),

where $F$ = flow in ml./hr., $V$ = volume (ml.), and $T_1$ = half life of RISA, i.e. at a constant flow rate $T_1$ is directly proportional to $V$.

Then, assuming a standard value of 50 ml. for $V$, the $T_{1/2}$ can be calculated for each patient. This is an artificial concept and represents the time taken for the initial concentration of RISA to fall to 50% if the ventricular volume had been 50 ml. (Fig. 2). The flow of CSF from the ventricle was also calculated from the above formula and expressed as ml./24 hr.

results

All the patients had an Arnold-Chiari malformation with an associated myelomeningocele. The site of the back lesion was thoraco-lumbar in 7, lumbar in 2, lumbo-sacral in 4, and in one patient the defect was extensive and involved the thoracic, lumbar, and sacral vertebrae. 10 of the patients were female. 19 RISA clearance tests were made in a series of 14 patients. In a group of 10 patients with progressive hydrocephalus the first test was carried out during the first two weeks of life after surgical closure of the myelomeningocele (Table I, II).

In 7 patients the test was carried out after establishing a ventriculo-atrial shunt, using either a low or medium pressure Spitz-Holter valve (Table III).

In Cases 4, 5, and 9 serial observations of the RISA clearance test were made and compared with the clinical course of the hydrocephalus as assessed by serial measurements of the skull circumference (Fig. 3, 4, and 5).

In Case 13, on open ventricular drainage with a Spitz-Holter valve in situ, it was possible to compare the volume of CSF lost (156 ml.) with the calculated volume lost (168 ml.) by measuring the activity of successive samples of CSF (Fig. 6).

Discussion

RISA when injected into a lateral cerebral ventricle disappears in an exponential fashion (Sweet

| TABLE I 
| Relation of Ventricular Volume, as Determined by RISA Clearance Test, to Skull Circumference |
|---|---|---|
| Case No. | Ventricular Volume (ml.) | Air Ventriculogram | Skull Circumference (cm.) |
| 1 | 56 | Grade I | 35-5 |
| 2 | 75 | Grade I | 35-5 |
| 3 | 108 | Grade II | 37 |
| 4 | 122 | Grade II | 35 |
| 5 | 123 | Grade II | 38-8 |
| 6 | 150 | Grade III | 38 |
| 7 | 175 | Grade III | 35-5 |
| 8 | 200 | Grade III | 34-2 |
| 9(a) | 335 | Grade III | 39-5 |
| 9(b) | 480 | Grade III | 43-2 |
| 10 | 340 | Grade III | 38 |
and Locksley, 1953; Sweet, Brownell, Scholl, Bowsher, Benda, and Stickly, 1954). This is due to the egress of the CSF through the normal pathways to the basal cisterns. By modern techniques using external γ scintillation scanograms, this movement has been noted to occur within a few minutes of the intraventricular injection (Di Chiro, 1964). However, there is also a transfer of the protein across the ependyma into the brain tissue, which then comes into equilibrium with the ventricular CSF protein. This transfer has been investigated by autoradiographic techniques (Bowsher, 1957; Lee and Olszewski, 1960). In the hydrocephalic infant with partial or complete obstruction to the anatomical pathways of the CSF and flattening of the ependymal cells (Bering, 1962), it might be expected that a high rate of absorption would be required to equilibrate the injected RISA with the brain tissue (Atkinson and Foltz, 1962). Our observations have not confirmed these findings, as the loss of protein from serial ventricular CSF samples has been by a single exponential system (Fig. 2 and 6). This difference may be due to one of several reasons: first, the range of ages in the two series was different, and secondly, there is evidence that the CSF dynamics in the hydrocephalic infant with a rapidly expanding skull differs from the adult with a rigid skull (J. R. Atkinson, 1965, personal communication).

A major source of error in the interpretation of data derived from previous isotope experiments is the failure to take into account the volume of the fluid compartment in which the exchanges occur (Selverstone, 1958). This is particularly important

### TABLE II

**Rate of Flow of CSF from Ventricle in 10 Cases of Arnold-Chiari Syndrome**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>$T_1^*$ (hr.)</th>
<th>$T_1^{0*}$ (hr.)</th>
<th>Rate of Flow (ml./24 hr.)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18</td>
<td>16-1</td>
<td>52</td>
<td>Progressive hydrocephalus; V-A shunt</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>18-5</td>
<td>46</td>
<td>Progressive hydrocephalus; meningitis; ventricular drainage; died</td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>24-5</td>
<td>34</td>
<td>Progressive hydrocephalus; V-A shunt</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>14-4</td>
<td>58</td>
<td>Progressive hydrocephalus; V-A shunt</td>
</tr>
<tr>
<td>5</td>
<td>35</td>
<td>14-2</td>
<td>58</td>
<td>Progressive hydrocephalus; V-A shunt</td>
</tr>
<tr>
<td>6</td>
<td>51</td>
<td>17</td>
<td>46</td>
<td>Progressive hydrocephalus; meningitis; died</td>
</tr>
<tr>
<td>7</td>
<td>56</td>
<td>16</td>
<td>53</td>
<td>Progressive hydrocephalus; bronchopneumonia; died</td>
</tr>
<tr>
<td>8</td>
<td>132</td>
<td>33</td>
<td>26</td>
<td>Developed progressive hydrocephalus after <em>Esch. coli</em> meningitis; V-A shunt</td>
</tr>
<tr>
<td>9</td>
<td>132</td>
<td>6</td>
<td>138</td>
<td>Progressive hydrocephalus; V-A shunt</td>
</tr>
<tr>
<td>10</td>
<td>104</td>
<td>14-8</td>
<td>56</td>
<td>Progressive hydrocephalus; V-A shunt</td>
</tr>
</tbody>
</table>

† Over-all mean rate of flow = 49 ml./24 hr. (S.E. ± 3 ml.)

† Excludes Case 9(a). * For definition of $T_1^*$ and $T_1^{0*}$ see text.

### TABLE III

**Rate of Flow of CSF from Ventricle in 7 Cases of Arnold-Chiari Syndrome with Functioning V-A Shunts**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>$T_1^*$</th>
<th>$T_1^{0*}$</th>
<th>Rate of Flow (ml./24 hr.)</th>
<th>CSF Pressure (mm.)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Functioning Low Pressure Spitz-Holter Valves</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>13</td>
<td>5-2</td>
<td>156</td>
<td>100-200</td>
<td>Arrested hydrocephalus after V-A shunt</td>
</tr>
<tr>
<td>12</td>
<td>50</td>
<td>3-7</td>
<td>223</td>
<td>100-200</td>
<td>Progressive hydrocephalus despite functioning V-A shunt; died</td>
</tr>
<tr>
<td>13</td>
<td>11</td>
<td>5-0</td>
<td>168</td>
<td>&gt; 200</td>
<td>Functioning V-A shunt; on open CSF drainage</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>6-7</td>
<td>125</td>
<td>100-200</td>
<td>Arrested hydrocephalus; ventricular catheter obstruction</td>
</tr>
</tbody>
</table>

Mean rate of flow = 168 ml./24 hr. (S.E. ± 21 ml.)

| **Functioning Medium Pressure Spitz-Holter Valves** | | | | | |
| 4        | 23      | 11-5      | 72                      | > 200              | Arrested hydrocephalus after V-A shunt |
| 14       | 23      | 8-8       | 94                      | < 100              | Progressive hydrocephalus despite functioning V-A shunt with low pressure, S-H valve changed to medium |
| 9        | 70      | 7-8       | 107                     | > 200              | Arrested hydrocephalus after V-A shunt |

Mean rate of flow = 91 ml./24 hr. (S.E. ± 13 ml.)

Over-all mean rate of flow = 135 ml./24 hr. (S.E. ± 20 ml.)
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PROGRESSIVE HYDROCEPHALUS - ARREST AFTER V-A SHUNT

Fig. 3.—Case 4. Correlation of skull circumference with CSF flow measurements (F = ml./hr.) before and after a ventriculo-atrial shunt.

Fig. 4.—Case 5. Correlation of skull circumference and CSF flow measurements, showing the effect of intermittent ventricular catheter obstruction by the choroid plexus.
Progressive Hydrocephalus Following Meningitis

Atwell and Scott

**PROGRESSIVE HYDROCEPHALUS FOLLOWING MENINGITIS**

**Fig. 5.** — Case 9. Correlation of skull circumference and CSF volumes and flow (F) measurements in patient who developed progressive hydrocephalus after Esch. coli meningitis, subsequently relieved by establishing a ventriculo-atrial shunt. 

(V = ventricular volume in ml. as determined by RISA clearance test.)

**Fig. 6.** — The exponential disappearance of RISA from the lateral ventricles in a patient on open CSF drainage. The calculated volume of CSF lost was 168 ml. compared to an actual loss of 156 ml.

in hydrocephalic infants with a dilated ventricular system (Table I). We have overcome this difficulty by determining the half life of the RISA for a ventricular volume of 50 ml. \(T_{1/2}\), and also by calculating the flow rate of CSF from the ventricles over a 24-hour period.

An objection to this method of investigating hydrocephalus is the need for repeated sampling of ventricular CSF, which is not without risk. This has been minimized by confining the sampling to 1, 4, and 24 hours. The reasons for selecting these intervals were discussed in detail by Atkinson and Foltz (1962). The use of a ventriculostomy reservoir inserted when the myelomeningocele is closed also increases safety. The reservoir may be modified for attachment of the Spitz-Holter valve when establishing the ventriculo-atrial shunt (Fig. 1).

One of the advantages of this RISA clearance test is the low dosage of 2 μc, which is required. This enables repeated observations to be made in the same patient (Fig. 3, 4, and 5), thus allowing each patient to act as his own control. This compares very favourably with RISA clearance tests using external counting or counting of blood samples, when the dose of RISA has to be increased to 20-100 μc.
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SKULL CIRCUMFERENCE; VENTRICULAR VOLUME; AIR VENTRICULOGRAPHY

Fig. 7.—The correlation of the ventricular volume (V) determined by the RISA clearance test with the dilatation of the ventricles seen in air ventriculography. Note the lack of correlation between skull circumference (SC) and ventricular size in Cases 6 and 10.


In infants with hydrocephalus due to the Arnold-Chiari malformation there is wide variation in the size of the cerebral ventricles as shown by air ventriculography (Lorber, 1961), the degree of hydrocephalus having been arbitrarily divided into three grades, grade I being the mildest with considerable brain tissue, whereas in grade III the cerebral cortex was only a few millimetres thick. Grade II fell between these two extremes. On the results of the RISA clearance test (Table I) the wide variation in ventricular volume is readily seen, as is the apparent lack of this correlation with skull size (Fig. 7). In addition Cases 6 and 10 would be classified on ventriculography as grade III (Fig. 7), though on the RISA clearance test their ventricular volumes differ by at least 100% (150 ml: 340 ml.). Therefore the RISA clearance test allows accurate assessment of the ventricular volume, and is of value in assessing the prognosis of these infants.

Partial obstruction of the exit foramina at the base of the brain and anomalies of the aqueduct are probably the main causes of the hydrocephalus in the Arnold-Chiari malformation. Infection and birth trauma may also be contributing factors. The results of the RISA clearance test in the first group of patients (Table I, excepting Case 9(a)) show a mean flow rate of 49 ml./24 hr. All these patients developed hydrocephalus which required ventriculo-atrial shunt. In Case 9 the clearance rate was 138 ml./24 hr., and progressive hydrocephalus did not develop until after meningitis, the flow rate then being reduced to 55 ml./24 hr. (Fig. 5). The RISA clearance test thus enables one to assess which patients will develop progressive hydrocephalus without natural arrest, thereby allowing the ventriculo-atrial shunt to be established at an earlier age.

On the basis of our results the criteria of progressive hydrocephalus without natural arrest has been a flow rate of less than 70 ml./24 hr.

The clinical improvement in the hydrocephalus following a ventriculo-atrial shunt correlates well with the results of the RISA clearance test—the mean rate of flow increasing from 49 to 135 ml./24 hr. (p < 0.001, see Table III). There is also a difference in the mean rate of flow using either a low or a medium pressure Spitz-Holter valve, though in this small series the difference is not highly significant (p < 0.05). In Case 14 with a functioning ventriculo-atrial shunt using a medium pressure Spitz-Holter valve, the hydrocephalus was still progressive.
but subsequently arrested on changing to a low pressure valve. This was probably due to the low CSF pressure (Table III). It has been shown by in vitro studies that the rate of flow through the valve is dependent upon the CSF pressure, and with pressures below 100 mm. H2O the flow was never above 25 ml./24 hr. (Forrest, 1962). It is a curious anomaly that while the rate of flow through a Spitz-Holter valve is dependent upon the CSF pressure, the formation of CSF is constant and independent of hydrostatic pressure, and is unaffected by the development of hydrocephalus (Bering and Sato, 1963).

Similar RISA clearance tests have been used to determine the patency of ventriculo-atrial and ventriculo-peritoneal shunts (Bell, 1959; Atkinson and Foltz, 1962). In the future this may be of considerable clinical importance, because of the grave long-term complications of ventriculo-atrial shunts (Friedman, Zita-Gozum, and Chatten, 1964; Erdohazi, Eckstein, and Crome, 1966). It may be possible to differentiate patients with functioning ventriculo-atrial shunts into two groups, first those who still require them to control the hydrocephalus, and a second group in whom the shunt may be safely removed due to the opening up of new CSF pathways. This could be carried out without surgical removal of the valve by doing a RISA clearance test before and after temporary occlusion of the atrial catheter.

Summary and Conclusions

A method using radio-iodinated serum albumin to measure the volume of the ventricular system, and the rate of disappearance of CSF from the lateral ventricles, has been described.

Newborn infants with a rate of flow less than 70 ml./24 hr. after surgical repair of the myelomeningocele will develop progressive hydrocephalus requiring a ventriculo-atrial shunt.

The test can be used to detect the patency of a ventriculo-atrial shunt, and may allow safe removal of the shunt in selected patients.

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