Formation of cerebrospinal fluid

Relation of studies of isolated choroid plexus to the standing gradient hypothesis

MICHAEL POLLAY, M.D.
Division of Neurosurgery, University of New Mexico School of Medicine, and Veterans Administration Hospital, Albuquerque, New Mexico

After a brief summary of current views on the origin of cerebrospinal fluid (CSF) and the processes underlying its elaboration, the author discusses studies of isolated choroid plexus in extracorporeal perfusion systems and flux chambers. The results suggest that transependymal water flow is secondary to the electrically silent pumping of sodium. The author presents evidence in support of the standing gradient hypothesis as the structural basis of CSF secretion.

KEYWORDS: CSF formation, choroid plexus perfusion, sodium pump, transepithelial water movement, standing gradient hypothesis, drug effects

The view held by Weed in 1914 concerning the intraventricular origin of cerebrospinal fluid (CSF) has for the most part survived the test of time and recurrent scrutiny, although contemporary understanding of the mechanism of formation is considerably greater. At the present time there is little question that CSF is a secretory product. This opinion is based not only on the differences in the ionic composition of this fluid as compared to an ultrafiltrate of plasma, but also on the characteristics of sodium movement between blood and the fluid within the ventricular system.

This report presents only a limited review of CSF physiology and includes a more detailed report on the characteristics of CSF formation as observed in the isolated choroid plexus.

Intraventricular CSF Formation

Table 1 presents a summary of the various methods used to measure the rate at which CSF is produced. The first three methods are the only ones suited for routine use in humans, and although less precise than the other methods listed, they have yielded similar results. The remaining methods, in addition to measuring the rate of fluid formation, have yielded important information concerning the absorptive capacity of choroid plexus and the mechanism underlying secretory and excretory function. The measurements of CSF formation in various species have for the most part been determined in ventriculocisternal perfusion systems (Fig. 1), the rate of accretion in the perfused ventricle being measured by the dilution of a nondiffusible marker in the perfu-
TABLE 1

Methods for measuring CSF formation

<table>
<thead>
<tr>
<th>Method (Ref)*</th>
<th>Calculation</th>
<th>Definition of Symbols†</th>
</tr>
</thead>
<tbody>
<tr>
<td>open drainage (30, 45)</td>
<td>( \dot{V}_t = \frac{V}{\Delta t} )</td>
<td>( V = ) volume of CSF collected; ( \Delta t = ) time</td>
</tr>
<tr>
<td>manometric (45)</td>
<td>( \dot{V}_t = \frac{\Delta V}{\Delta t} )</td>
<td>( \Delta V = ) volume removed; ( \Delta t = ) time required to re-establish original pressure after CSF drainage</td>
</tr>
<tr>
<td>radiographic (45, 46)</td>
<td>( \dot{V}_t = r A )</td>
<td>( r = ) the rate of ascent of air or lipoidal level in ventricle; ( A = ) cross-sectional area of ventricle</td>
</tr>
<tr>
<td>ventriculocisternal perfusion (10, 13, 23)</td>
<td>( \dot{V}_t = \dot{V}_i (C_i - C_o)/C_o )</td>
<td>( \dot{V}_i = ) rate of inflow; ( C_i = ) inflow concentration of marker; ( C_o = ) outflow concentration of marker</td>
</tr>
<tr>
<td>aqueduct-4th ventricle perfusion (43)</td>
<td>same as VC perfusion</td>
<td>—</td>
</tr>
<tr>
<td>choroid plexus in isolation chamber (35, 49)</td>
<td>same as VC perfusion</td>
<td>—</td>
</tr>
<tr>
<td>choroid plexus perfusion (44, 53)</td>
<td>( \dot{V}<em>t = Q_v (H</em>{ctv}/H_{ctv}) - 1 )</td>
<td>( Q_v = ) choroidal venous outflow rate; ( H_{ctv} = ) arterial and venous hematocrits</td>
</tr>
</tbody>
</table>

* See references at end of text.
† \( \dot{V}_t = \) rate of CSF formation (volume/unit time).

---

TABLE 2

CSF turnover and formation per tissue weight*

<table>
<thead>
<tr>
<th>Species (Ref)</th>
<th>CSF Turnover Rate (%/min)†</th>
<th>CSF Formation/Weight (µl mg⁻¹ min⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>man</td>
<td></td>
<td></td>
</tr>
<tr>
<td>adult</td>
<td>.37</td>
<td>.18 - .29</td>
</tr>
<tr>
<td>children</td>
<td>.26</td>
<td>—</td>
</tr>
<tr>
<td>(12, 28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>rhesus monkey</td>
<td>—</td>
<td>.13</td>
</tr>
<tr>
<td>(33, 34)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>goat</td>
<td>.65</td>
<td>.36</td>
</tr>
<tr>
<td>(23)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sheep</td>
<td>—</td>
<td>.13</td>
</tr>
<tr>
<td>(44)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dog</td>
<td>.40 - .60</td>
<td>.63 - .96</td>
</tr>
<tr>
<td>(36, 49)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cat</td>
<td>.40 - .50</td>
<td>.40 - .55</td>
</tr>
<tr>
<td>(15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>rabbit</td>
<td>.54 - .63</td>
<td>.37 - .43</td>
</tr>
<tr>
<td>(16, 53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>shark</td>
<td>.3</td>
<td>.05</td>
</tr>
<tr>
<td>(40)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Modified and expanded from Davson's and Cserr.†
† % of total CSF volume.

The two major approaches to the study of the site of ventricular fluid origin have involved either a study of isolated choroid plexus or observations on ventricular perfusion systems devoid of plexus tissue. The isolated plexus experiments in rabbit, cat, and dog seem to indicate that most, if not all, of CSF is derived from a choroidal source. Similar studies in sheep and rabbit, however, do not support this thesis. The strongest evidence presented in support of the extrachoroidal origin of CSF has been the measurement of CSF formation in cerebral ventricles not containing choroid plexus. In the rabbit, this was accomplished by perfusing only the aqueduct and anterior fourth ventricle, while in the monkey, the ventricles were perfused after choroid plexectomy. Using these methods, it appears as if 35% of the CSF in the rabbit and 70% of the CSF in the rhesus monkey are derived from non-
Cerebrospinal fluid formation

choroidal sources, presumably adjacent brain tissue (Table 3). The percentage of CSF formed by choroid plexus can also be estimated by comparing the total rate of fluid production in the intact ventricular system using ventriculocisternal perfusion, and the rate due to choroid plexus per unit weight of tissue, determined from studies on the isolated plexus. The difference between these two values would represent extrachoroidal fluid production (Table 3). At present, the results indicate that a significant portion of intraventricular CSF cannot be charged to the plexus; however, technical difficulties associated with the experimental methods do not allow precise quantitation.

Extracorporeal Perfusion of the Isolated Choroid Plexus

Method and Basic Observations

In 1972, our laboratory developed a method in which the choroid plexus of sheep could be maintained satisfactorily in an extracorporeal perfusion system for up to 7 hours; this experimental system has been presented elsewhere in great detail and will only be briefly described at this time. Arterial inflow to the plexus was controlled by means of a catheter in the internal carotid artery after ligation of all its branches except the anterior choroidal artery. Venous outflow from the plexus was collected from a catheter in the external carotid artery after ligation of all its branches except the anterior choroidal artery. Venous outflow from the plexus was collected from a catheter

**Table 3**

<table>
<thead>
<tr>
<th>Animal</th>
<th>Perfusion Method</th>
<th>Rate of Extrachoroidal Formation (μl/min)</th>
<th>% of Total CSF Production*</th>
</tr>
</thead>
<tbody>
<tr>
<td>rabbit</td>
<td>aqueductal</td>
<td>4.23</td>
<td>34.9</td>
</tr>
<tr>
<td>dog</td>
<td>ventricular</td>
<td>7.90</td>
<td>21.5</td>
</tr>
<tr>
<td>goat</td>
<td>ventricular</td>
<td>14.85</td>
<td>8.2</td>
</tr>
<tr>
<td>monkey</td>
<td>ventricular</td>
<td>13.30</td>
<td>69.2</td>
</tr>
</tbody>
</table>

* Intraventricular only.
† Plexectomized animals or perfusion of nonchoroidal portion of ventricular system.
‡ Based on rate of formation by plexus of 0.37 μl mg⁻¹ min⁻¹ subtracted from total intraventricular rate of CSF formation.}

**Table 4**

<table>
<thead>
<tr>
<th>Perfusion Method</th>
<th>choroid artery pressure (mm Hg)</th>
<th>choroid arterial blood flow (μl min⁻¹)</th>
<th>choroid venous blood flow (μl min⁻¹)</th>
<th>CSF formation (μl min⁻¹)</th>
<th>net sodium flux (mEq/min)</th>
<th>net chloride flux (mEq/min)</th>
<th>CSF [Na⁺]/plasma [Na⁺]</th>
<th>CSF [Cl⁻]/plasma [Cl⁻]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aqueductal</td>
<td>93</td>
<td>245.2</td>
<td>232.3</td>
<td>12.9</td>
<td>2.04</td>
<td>1.65</td>
<td>1.038 (1.05)</td>
<td>1.098 (1.05)</td>
</tr>
<tr>
<td>Ventricular</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Data represent mean values from 50 experiments. Results in part from Reference 44 based on smaller number of experiments.
† Values in parentheses represent ratio expected of an ultrafiltrate of plasma.
in the internal cerebral vein at the level of the foramen of Monro. The vascular perfusion fluid consisted of doubly filtered blood with a hematocrit half of normal. The fluid bathing the plexus was artificial CSF maintained at a temperature similar to that of the blood (38°C). Both physiological fluids have a composition and acid-base status comparable to that normally found in sheep. The measurement of CSF formation in this preparation was based on the assumption that equal volumes of the red blood cells entered and left the plexus and that the volume flow across the lamina epithelialis was reflected by the inequality between arterial and venous blood flow. In view of some of the uncertainties associated with the control of the territory irrigated by the anterior choroidal artery (even with ligation of all visible branches), the calculated rate of CSF formation was based on the venous outflow from the plexus (line 7, Table 1). In some 50 experiments, we calculated a rate of CSF production of almost 13 µl/min when the perfusion pressure was 90 to 100 mm Hg and choroidal artery blood flow 2.9 µl/mg·min⁻¹. The true concentrations of sodium and chloride in the nascent fluid were computed from the net flux of each ion divided by the net flux of water; the concentration for sodium was 158 mEq/l and for chloride 127.9 mEq/l. The ratio of the concentration in CSF to concentration in plasma was in both cases greater than that which might be expected in a simple ultrafiltrate of plasma (Table 4). Although our value for net water transport across the choroidal ependyma of sheep (0.13 µl/mg·min⁻¹) is less than that reported for rabbit, it is approximately the same as that presented for rhesus monkey. Transependymal water transport continued into a hypotonic media in both sheep and rabbit, although at a reduced rate. In our preparation we were unable to demonstrate a transepithelial potential, although a small potential difference (PD) might well have been overlooked due to technical difficulties. In recent studies utilizing the choroid plexus of frog and cat as occluding membranes in flux chambers, a very small PD (< 1.0 mV) has been observed. It is now generally appreciated that the large CSF-to-blood potential (ventricular CSF-to-jugular venous blood) is not related to solute transport across the lamina epithelialis.

**Effect of Drugs on CSF Secretion**

The effect of drugs on CSF secretion by the isolated plexus has yielded important information concerning the underlying mechanism of secretion. Table 5 is a compilation of conditions that may alter CSF formation. Most of the drug and environmental effects are due to: 1) interference with cellular respiration, produced by dinitrophenol, hypoxia, or hypothermia; 2) inhibition of carbonic anhydrase by acetazolamide or furosemide; 3) inhibition of sodium-potassium (Na-K) activated adenosine triphosphate (ATPase) by cardiac glycosides and certain steroids; and 4) destruction of plexus tissue by irradiation, plexectomy, or pressure.

In this report we will only discuss two classes of drugs in detail, although valuable information has also been gained by study of other conditions that affect volume flow across the plexus epithelium. In our original studies on sheep choroid plexus, for instance, we demonstrated that Diamox (acetazolamide), contained either in CSF bathing the plexus (10⁻³ M), or in blood perfusing the plexus (20 µg/cm³), rapidly (< 15 min) resulted in complete cessation of CSF production. In later experiments, the similar effect of ouabain was observed, regardless of whether it was in the bathing medium (10⁻⁴ M) or blood (10⁻⁵ M).

**Carbonic Anhydrase.** The effect of carbonic anhydrase inhibitors on CSF formation is well known, although its mode of action on the secretory mechanism remains unclear. In equivalent concentrations this drug appears to be more effective in decreasing the secretory activity of the isolated plexus (virtually 100%) than in decreasing fluid formation in the intact ventricular system. Most proposed explanations of the mode of action of these drugs are based on their role in the hydration of carbon dioxide (CO₂). One proposal, which suggested that sodium, chloride, and obligated water are exchanged for products derived from the hydration of CO₂, was not supported by the analysis of bicarbonate content of choroidal venous blood, since the amount of the latter was insufficient to explain the observed sodium and chloride flux. Nor could we prove that the decrease in CSF formation was due to increased choroidal vascular resistance secondary to elevation of pCO₂. Measurement of...
Cerebrospinal fluid formation

### TABLE 5

<table>
<thead>
<tr>
<th>Drug or Experimental Conditions</th>
<th>Type of Measurement*</th>
<th>Remarks†</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>acetazolamide, IV</td>
<td>Choroidal 85</td>
<td></td>
<td>1, 10, 11</td>
</tr>
<tr>
<td>acetazolamide, CSF</td>
<td>Non-Choroidal 54</td>
<td></td>
<td>1, 10, 11</td>
</tr>
<tr>
<td>ouabain, IV</td>
<td>Both 50</td>
<td>0.05 mg/kg</td>
<td>10, 11, 17</td>
</tr>
<tr>
<td>ouabain, CSF</td>
<td>Choroidal 90+</td>
<td></td>
<td>10, 11, 53</td>
</tr>
<tr>
<td>ouabain, CSF</td>
<td>Non-Choroidal 40</td>
<td>10⁻⁴ to 10⁻⁵ M</td>
<td>39</td>
</tr>
<tr>
<td>Digoxin, IV</td>
<td>Both 145</td>
<td></td>
<td>37</td>
</tr>
<tr>
<td>dinitrophenol, CSF</td>
<td>Both 78</td>
<td>therapeutic dose (human)</td>
<td>10, 13, 15</td>
</tr>
<tr>
<td>norepinephrine, CSF</td>
<td>Both 190+</td>
<td></td>
<td>10, 13, 51</td>
</tr>
<tr>
<td>amphotericin B</td>
<td>Both 70</td>
<td>CSF 1 mg % IV 10⁻⁵ M</td>
<td>17, 21</td>
</tr>
<tr>
<td>spironolactone</td>
<td>Both 71</td>
<td>CSF 50 mg % IV 5 mg/min</td>
<td>17, 21</td>
</tr>
<tr>
<td>ethacrynic acid</td>
<td>Both 760</td>
<td>IV 5-10 mg/kg</td>
<td>21, 36</td>
</tr>
<tr>
<td>vasopressin</td>
<td>Both 50</td>
<td>IA .3V/min</td>
<td>17, 21</td>
</tr>
<tr>
<td>furosemide</td>
<td>Both 45</td>
<td>IV 20-50 mg/kg</td>
<td>6, 21, 48, 50</td>
</tr>
<tr>
<td>cortisone and other steroids</td>
<td>Both 35</td>
<td>IM 20 mg/kg/doz</td>
<td>22, 31, 52</td>
</tr>
<tr>
<td>pH changes ↑↓</td>
<td>Both 50</td>
<td>requires marked changes in pH</td>
<td>38</td>
</tr>
<tr>
<td>PaCO₂↑†</td>
<td>Both 23</td>
<td></td>
<td>2, 17</td>
</tr>
<tr>
<td>PaCO₂↓†</td>
<td>Both 23</td>
<td></td>
<td>17</td>
</tr>
<tr>
<td>altered CSF or blood</td>
<td>Both 60-80</td>
<td>11.3% C/° between 31-41°C</td>
<td>18</td>
</tr>
<tr>
<td>osmolality</td>
<td>Both 3.3 X 10³ μl/min/cm²/mm Hg</td>
<td>11, 23, 55</td>
<td></td>
</tr>
<tr>
<td>hydrocephalus</td>
<td>Both 45-52</td>
<td>in some experiments no change</td>
<td>3, 25, 49, 50</td>
</tr>
<tr>
<td>choroid plexectomy</td>
<td>Both 32</td>
<td></td>
<td>33, 34</td>
</tr>
<tr>
<td>irradiation</td>
<td>Both 50-62</td>
<td>rhenium 188 in CSF, 800 μc dose</td>
<td>8</td>
</tr>
<tr>
<td>immaturity</td>
<td>Both 50-80</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>hypoxia</td>
<td>Both 33</td>
<td>dogs breathing 5% O₂ in nitrogen</td>
<td>26, 32</td>
</tr>
<tr>
<td>hypervitaminosis A</td>
<td>Both 30</td>
<td>10.8 gm vitamin A/kg/day</td>
<td>27</td>
</tr>
</tbody>
</table>

* Results given in % change from normal. Choroidal = measurements made on isolated plexus; nonchoroidal = based on studies of ventricular system without plexus tissue; both = measured in intact ventricular system.

† IV = intravenous; IA = intraarterial; IM = intramuscular.

Choroidal artery blood flow and pressure in the isolated plexus of sheep was unchanged by Diamox in either the CSF or blood.44

The most recent study concerned with clarifying the role of CO₂ hydration in CSF formation was carried out in the dogfish by Maren.29 The central role of bicarbonate (HCO₃⁻) in the secretory process was based on the observation that the rapid accession of HCO₃⁻ to the CSF was inhibited by acetazolamide to a degree similar to that of sodium and water. It was proposed that the secretory cells of the plexus engage in the protolysis of water. The hydroxyl ion (OH⁻) formed by this process would then react with CO₂, either with or without carbonic anhydrase, to form HCO₃⁻ and H⁺; the proton would then enter blood and be buffered. An HCO₃⁻ gradient would be established and sodium would serve as a counter ion for transport. Since these two ions would be intimately coupled, anything that would interfere with ATPase or carbonic anhydrase activity would produce similar changes in both sodium and water transport. The best evidence against this proposed role of carbonic anhydrase in water transport is the observed uncoupling between water and sodium flux in the presence of Diamox.12,17 Maren29 believes that the relative inefficacy of Diamox or sodium transport as compared to water movement is an illusion based on transfer constants determined without proper evaluation of timing of dose (in relation to measurements), fate of drug, and volume characteristics of the fluid compartments.

**Cardiac Glycosides.** The mode of action of cardiac glycosides on CSF formation is better understood than that of carbonic anhydrase inhibitors.1,10,11,17,20 These glycosides inhibit the Na-K ATPase enzyme that is required for
the hydrolysis of ATP. Since most secretory processes involve the active transport of Na⁺ or K⁺, the presence and localization of this enzyme is central to the understanding of the mechanism of fluid secretion and its structural basis. It has been demonstrated that the choroid plexus contains this enzyme and that fluid production in the isolated plexus is completely inhibited by ouabain, either in blood or bathing media. The glycosides appear to have less effect on CSF formation in the total CSF system; in some studies they were only effective in CSF. The binding of H³ ouabain to membrane-bound Na-K ATPase in frog choroid plexus suggests that sodium pumps may be present only at the brush border of the ependymal cell. The absence of ouabain binding to the basolateral membranes may be the result of ouabain inhibiting sodium pumps only on the side of the membrane to which sodium is pumped. Definitive localization of these pumps will be necessary to justify acceptance of any of the currently proposed models of solute-solvent coupling.

**Structural Basis of CSF Formation**

**Double Membrane Model**

Patlak, et al., who also quote from the comparable theories of Curran, have described a double-membrane model to account for iso-osmotic water transport found in various absorptive epithelia (Fig. 2). The first membrane is relatively impermeable to the transported ion, while the second is highly permeable to the solute. The active transport of the solute across the first membrane results in the establishment of an osmotic gradient and a secondary flow of water into the second chamber (II). The hydrostatic pressure thus developed leads to a flow of isotonic fluid across the highly permeable membrane separating Chambers II and III.

**Standing Gradient Hypothesis**

This model has now been extended to secretory epithelia; here the plication of the basal cell surfaces would serve as sites of standing osmotic gradients since most secretory epithelia lack extensive intercellular compartments. As noted by Oschman and Berridge, the basic problem is to explain how solute and water interact at two interfaces. In Fig. 3, we have applied the Diamond and Bossert principles of the standing gradient hypothesis to the choroidal ependyma. The anatomy of the choroid plexus will not be reviewed here, but excellent histological studies have demonstrated the tight junction connecting adjacent choroidal ependymal cells, as well as the large fenestrated capillaries in the plexus. In our proposed model, the first step in the formation of CSF would be the transcapillary movement of an ultrafiltrate of plasma under
the influence of a hydrostatic gradient. This filtrate would then enter the basal infoldings of the choroidal cell (backward channels) after the larger particles had been filtered by the basement membrane. As the filtrate enters these channels it is isotonic to blood; with the active transport of sodium into the cell, the fluid in the channel becomes hypotonic as it approaches the blind end of the channel, thus establishing a favorable osmotic gradient for water flow into the cell. A similar process occurring within the intercellular clefts (between adjacent choroidal cells but proximal to the tight junctions) is quite possible. In either case, this is the first interface where water and the major transported ion interact. The second interface would be the apical surface of the choroidal cell, which is also highly folded. A similar mechanism would then operate to couple solute and solvent movement into the ventricular system via the forward (microvilli) channels.

Until it becomes possible to sample extrachoroidal spaces, it will remain difficult to test this model directly. Certain observations, however, do support this proposed model. The first of these is the observed secretion of CSF into a hypotonic medium (uphill transport of water). This supports the contention that, at least at the apical interface, the fundamental process requires the expenditure of energy for the transapical solute (sodium) movement. In addition, the proposed model is supported by the observation that alteration in solute and solvent movement leads to accumulation of fluid at the intercellular regions. Burgess and Segal have demonstrated the dilatation of the intercellular clefts of choroidal epithelium when fluid secretion was inhibited by Diamox or ouabain; this could be expected since the flow of water is opposite in direction to that in choroid plexus. The same observation has been made in the gallbladder with collapse of intercellular clefts.

References

1. Ames A 3rd, Higashi K, Nesbett FB: Effects of 
   PCO₂, acetazolamide and ouabain on
   volume and composition of choroid-plexus
   fluid. J Physiol (Lond) 181:516-524, 1965
2. Ames A 3rd, Sakanoue M, Endo S: Na, K,
   Ca, Mg, and Cl concentrations in choroid
   plexus fluid and cisternal fluid compared
   with plasma ultrafiltrate. J Neurophysiol
   27:672-681, 1964
   in formation and absorption of cerebrospinal
   fluid within the cerebral ventricles. J
   Neurosurg 20:1050-1063, 1963
4. Bito LZ, Davson H: Local variations in
   cerebrospinal fluid composition and its
   relationship to the composition of the ex-
   tracellular fluid of the cortex. Exp Neurol
   14:264-280, 1966
5. Brightman MW: The distribution with the
   brain of ferritin injected into cerebrospinal
   fluid compartments. J. Ependymal distribu-
6. Buhrley LE, Reed DJ: The effect of
   furosemide on sodium-22 uptake into
   cerebrospinal fluid and brain. Exp Brain Res
   14:503-510, 1972
7. Burgess A, Segal MB: Morphological changes
   associated with inhibition of fluid transport in
   the rabbit choroid plexus. J Physiol (Lond)
   208:88P-91P, 1970
8. Carter TF, Bardfeld PA, Shulman K: The up-
   take of Rhenium 188 in the choroid plexus and
   its effect on CSF production, in Harbert JC
   (ed): Cisternography and Hydrocephalus.
   Springfield, Ill, Charles C Thomas, 1972, pp
   131-142
   Prog Brain Res 29:135-146, 1968
10. Cserr HF: Physiology of the choroid plexus.
    Physiol Rev 51:273-311, 1971
11. Curl FD, Pollay M: Transport of water and
    electrolytes between brain and ventricular
    fluid in the rabbit. Exp Neurol 20:558-574,
    1968
    tion and absorption of cerebrospinal fluid in
13. Davson H: Physiology of the Cerebrospinal
14. Davson H, Bradbury M: Formation and
    drainage of the cerebrospinal fluid basic con-
    cepts, in Brooks CMC, Kao FF, Lloyd BB
    (eds): Cerebrospinal Fluid and the Regulation
    of Ventilation. Philadelphia, Davis, 1965, pp
    385-395
15. Davson H, Kleeman CR, Levin E: Quan-
    titative studies of the passage of different sub-
    stances out of the cerebrospinal fluid. J
    Physiol (Lond) 161:126-142, 1962
16. Davson H, Pollay M: Influence of various
    drugs on the transport of ³¹ I and PAH across
    the cerebrospinal fluid-blood barrier. J Physiol
    (Lond) 167:239-246, 1963
17. Davson H, Segal MB: The effects of some in-
    hibitors and accelerators of sodium transport
    on the turnover of ²² Na in the cerebrospinal
35. Miner LC, Reed DJ: Composition of fluid obtained from choroid plexus tissue isolated in a chamber in situ. J Physiol (Lond) 227:127–139, 1972
50. Shaywitz BA, Katzman R, Escriva A: CSF
formation and $^{24}$Na clearance in normal and hydrocephalic kittens during ventriculocisternal perfusion. Neurology (Minneap) 19:1159–1168, 1969


This work was supported in part by Public Health Service Grant NS09002.
A summary of this work was presented at the Second International Symposium on Intracranial Pressure in Lund, Sweden, June, 1974.
Address reprint requests to: Michael Pollay, M.D., University of New Mexico School of Medicine, 915 Stanford Drive, N.E., Albuquerque, New Mexico 87131.