Potassium exchange between cerebrospinal fluid, plasma, and brain

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METHODS

General. Steady state fluxes of test substances into or out of the ventricular systems of anesthetized dogs and rats were measured using the technique of ventriculocisternal perfusion. Perfusion inflow rates were approximately 0.9 ml/min in dogs and 0.02 ml/min in rats, the precise rates of both inflow and outflow being determined gravimetrically in each experiment. Ionic composition (in mEq/liter) of the perfusion fluid was as follows, except where otherwise indicated: Na, 150; K, 3.0; Ca, 2.3; Mg, 1.6; Cl, 135; HCO3, 25; and PO4, 0.5. The fluid was equilibrated with 5% CO2. Inulin (40 mg/100 ml) and creatinine (50 mg/100 ml) were always added to the perfusion reservoir; inulin clearance was used to calculate rates of formation and absorption of CSF, as described by Heisey et al. (8); creatinine outflux served as a measure of passive, nonspecific permeability in each animal, as described below. Trace quantities of K42, Na24, Na22, or Cl36 were added to the perfusion fluid when indicated.

Operative procedures. Mongrel dogs (5-15 kg) or female white rats (200-300 g) were anesthetized with sodium pentobarbital (30 mg/kg). Full surgical anesthesia was maintained by supplementary doses of sodium pentobarbital (dogs) or ether (rats) throughout the experiment. For ventriculocisternal perfusions, one hypodermic needle was introduced through a guide tube previously cemented to the atlanto-occipital membrane. In dogs, the cisternal needle was introduced through a guide tube previously cemented in position over the atlando-occipital membrane. In rats, a 1/2 inch 26 gauge needle was lowered into the cisterna magna and then attached to the skull with cement. The cisternal needle and associated outflow tubing were filled with artificial spinal fluid before the puncture, successful puncture being indicated by the appearance of pulsations in fluid within the tubing. In dogs, the lateral ventricle was punctured with a 1 1/4-inch 21-gauge needle lowered into the ventricle on a stereotaxic device and then attached to the skull with cement. The cisternal needle and associated outflow tubing were filled with artificial spinal fluid before the puncture, successful puncture being indicated by the appearance of pulsations in fluid within the tubing. In dogs, the lateral ventricle was punctured with a 1 1/4-inch 21-gauge needle lowered into the ventricle on a stereotaxic device; in rats, a 1/2-inch 26-gauge needle was used. Successful placement of the needles was indicated by normal creatinine outflux and by low fluid pressure measured at the inflow to the ventricular needle during

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perfusion. Methylene blue was added to the perfusion fluid at the end of each experiment and the brain examined in order to verify proper placement of the cisternal and ventricular needles.

The brain plus approximately 1 cm of attached spinal cord were dissected out of rats for analysis of K\textsuperscript{42} and Na\textsuperscript{22}. In order to remove as much CSF as possible the ventricles were exposed by dissection and blotted.

Analytical methods. Creatinine was determined colorimetrically as the alkaline picrate at 520 m\(\mu\) in inulin as fructose by the resorcinol method (23), chloride with the Aminco-Cotlove automatic chloride titrator (4), and potassium and sodium with a flame photometer. K\textsuperscript{42}, Na\textsuperscript{24}, and Na\textsuperscript{22} were counted in a crystal-scintillation well counter. Samples containing C\textsuperscript{13} were pipetted into a glass vial. Corrections were made for self-absorption.

Weighed brain and cord tissue was digested for 1 hr in approximately 10 vol of boiling concentrated nitric acid. Aliquots of this digest were analyzed for isotope. Mean (± se) weight of the rat brains analyzed was 1.83 ± .06 g.

Drugs, intravenous infusions (dogs). A 10\textsuperscript{-2} M stock ouabain solution was prepared with crystalline ouabain in 0.9 Yo saline. A concentrated solution of the commercially available sodium salt of acetazolamide was freshly prepared by dissolving anhydrous acetazolamide in distilled water.

In the steady state, net outflux, \(\dot{i}\), may also be defined as the difference between the unidirectional transependymal transport via ionic (or molecular) transport out of ventricular CSF, \(\dot{i}\), and fluid formed in bulk, respectively.

\[\dot{n} = \dot{V}_i(c_i - c_f) - (\dot{V}_o + C_{i\text{in}})(c_o - c_f) \]  

where

\(\dot{n}\) = rate of net transependymal transport via ionic (or molecular) transport out of ventricular CSF, \(\mu M/min\)
\(c = \) concentration, mmolal
\(V = \) rate of flow, ml/min
\(C_{i\text{in}} = \) inulin clearance = (\(\dot{V}_i c_i - \dot{V}_o c_o\))/\(c_o\) and is identical with rate of bulk CSF absorption as described in ref. 0
\(i, o, f = \) subscripts denoting inflow fluid, outflow fluid, and fluid formed in bulk, respectively.

In the steady-state, net outflux, \(\dot{n}\), may also be defined as the difference between the unidirectional transependymal fluxes between CSF and blood, steady state being defined in terms of constant concentration of the test material in tissues interposed between blood and CSF.

\[\dot{n} = k_0 c_o - k_1 c_p \]  

where

\(k_0, k_1 = \) unidirectional flux coefficients describing steady-state transport into and out of ventricular CSF, respectively, ml/min
\(c_o, c_p = \) plasma and mean ventricular concentrations, respectively, mmolal; \(c_v = c_o + .37 (c_i - c_o)\) as described in ref. 19.

Combining equations 1 and 2 and solving for the influx coefficient, \(k_i\), we have

\[k_i = k_o c_v - (\dot{V}_i(c_i - c_f) - (\dot{V}_o + C_{i\text{in}})(c_o - c_f)) / c_p \]  

Number of observations used to determine mean value given in parentheses. * From Heisey et al. (8).

Calculations. Equations describing net flux of any test material into or out of ventricular perfusion fluid have been derived by Pappenheimer et al. (18). Net transependymal flux is given by

\[\dot{n} = \dot{V}_i(c_i - c_f) - (\dot{V}_o + C_{i\text{in}})(c_o - c_f) \]  

Table 1. Sample data and calculations for dog 50

<table>
<thead>
<tr>
<th>Species</th>
<th>Flux Coefficient, ml/min (Mean ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outflow coeff.</td>
<td>Na</td>
</tr>
<tr>
<td>Rat</td>
<td>0.0031±.0002</td>
</tr>
<tr>
<td>Dog</td>
<td>0.003±.0007</td>
</tr>
<tr>
<td>Goat*</td>
<td>0.005±.0005</td>
</tr>
</tbody>
</table>

Number of observations used to determine mean value given in parentheses. * From Heisey et al. (8).

<table>
<thead>
<tr>
<th>TABLE 2. Transependymal flux coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Rat</td>
</tr>
<tr>
<td>Dog</td>
</tr>
<tr>
<td>Goat*</td>
</tr>
</tbody>
</table>

Number of observations used to determine mean value given in parentheses. * From Heisey et al. (8).
TABLE 3. Effects of acetazolamide on bulk CSF secretion and on K flux coefficients in anesthetized dogs

<table>
<thead>
<tr>
<th>Rate of Bulk</th>
<th>K Influx</th>
<th>K Outflux</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.000±0.002</td>
<td>1.54±0.013</td>
</tr>
<tr>
<td>Acetazol. iv</td>
<td>0.022±0.004</td>
<td>1.54±0.007</td>
</tr>
<tr>
<td>Acetazol. in CSF</td>
<td>0.020±0.004</td>
<td>1.54±0.007</td>
</tr>
</tbody>
</table>

Values are means ± SE and are expressed in ml/min.

In the special case when a test substance is added only to the perfusion fluid, \( c_p \) and \( c_i \) are zero and equation 3 reduces to the expression for outflux coefficient given by Heisey et al. (8).

\[
k_o = \frac{V_i \cdot c_i - (V_a + C_n) c_o}{c_v} \tag{4}
\]

Thus, \( k_o \) can be determined from equation 4 by adding a test material to the perfusion reservoir and determining \( V_i, V_a, c_i, c_o, \) and \( C_n \). When the test material is normally present in plasma, \( k_o \) may still be determined from equation 4 if an isotope of the test substance is added to the perfusion fluid. Once the value of \( k_o \) has been determined, the value of \( k_i \) can be calculated from equation 3 using data obtained when the test substance is present in both plasma and CSF. For this purpose it is necessary to assume a value for \( c_i \), i.e., for the concentration in fluid formed in bulk. Ames et al. (1) have shown that sodium and chloride are present in freshly formed choroid plexus fluid in approximately the same concentration as in plasma, and it will be assumed that \( c_i = c_p \) in computing influx coefficients for these ions. In the case of potassium, the concentration in fluid secreted by the plexuses remains close to 3 mmolal even when plasma concentration is varied (Ames, personal communication). Thus, \( c_i \) for potassium will be assumed to be 3.0; however, the exact value assumed has little effect on calculated influx coefficients since only a small fraction of total potassium influx can be accounted for by bulk secretion.

It should be emphasized that the flux coefficients, \( k_o \) (equation 4) and \( k_i \) (equation 3), are defined only for steady-state exchange between CSF and plasma. When a test material is first added to the perfusion fluid and crosses the ependymal linings of the ventricle, it can be either stored in brain or carried off by blood in capillaries near the ventricular surface. It can be anticipated that test materials which are largely restricted to extracellular fluid will equilibrate rapidly with brain tissue immediately surrounding the ventricles, and after this initial period of equilibration, steady-state conditions will be attained. However, an ion such as potassium may take many hours to equilibrate with brain tissue. In this case the transependymal outflux coefficient, \( k_o \), can still be calculated but it will not refer to flux from CSF to plasma. It follows that the influx coefficient, \( k_i \), calculated from equation 3 during the unsteady state will be a virtual quantity; nevertheless, it is valuable as a measure of the approach to the steady state. In order to avoid confusion, the value of \( k_i \) determined during the unsteady state will be designated \( k_i' \) (the apparent influx coefficient from plasma to CSF).

RESULTS

Normal flux coefficients. Typical primary data obtained from ventriculocisternal perfusion are shown in Table 1 together with the derived values of fluid formation, bulk absorption, and the flux coefficients for potassium and creatinine. Mean values of flux coefficients for creatinine, Na+, Cl−, and K+ are summarized in Table 2. Values published previously for unanesthetized goats (8) are included for comparison. The results show that outflux coefficients for potassium are about 4 times greater than for sodium in all three species.

Mean (± SE) normal rate of bulk CSF secretion was 0.15±0.021 ml/min in dogs and 0.022±0.003 ml/min in rats. Comparison of rates of CSF formation with the transependymal potassium influx coefficients shows that the contributions of bulk formation and ionic transport to total potassium influx are very different. Less than 2% of total influx is attributable to potassium contained in freshly formed choroid plexus fluid, the remaining 80% being derived from the large ionic influx (see sample calculation of percent influx from bulk secretion in Table 1). The ionic component of potassium exchange is unaffected by inhibition of choroid plexus secretion by acetazolamide, as shown in Table 3. Under these conditions, ionic transport processes account for more than 90% of total potassium exchange with ventricular CSF.

The data referring to anesthetized dogs shown in Table 2 were obtained during the first 2 hr of ventriculocisternal perfusion. Continued perfusion is usually accompanied by a gradual increase in the passive permeability of the ventricular system. The outflux coefficient for creatinine is approximately doubled after 4–6 hr of perfusion, as shown in Fig. 1, and permeability to sodium and chloride increases proportionately, as shown in Fig. 2. The progressive increase in creatinine outflux presumably results from the approach to the steady state. In order to avoid confusion, the value of \( k_i \) determined during the unsteady state will be designated \( k_i' \) (the apparent influx coefficient from plasma to CSF).
In addition to inhibiting the active component of potassium outflux, perfusion of the ventricular system with 10^{-6} \text{M} ouabain caused several other effects. The positive d-c potential between CSF and blood was reduced, as described by Held et al. (9), and mean (± SE) rate of CSF production was decreased from the control value of 0.35 ± 0.02 to 0.10 ± 0.002 ml/min (N = 8). Ouabain has been shown to inhibit CSF production in cats (25) and rabbits (27), but Oppelt et al. (15, 16) were unable to demonstrate inhibition in dogs. It is possible that the ouabain perfusions used by Oppelt et al. were not of sufficient duration to detect the inhibition. In my experience inhibition could not usually be detected until 80–120 min after addition of ouabain to the perfusion fluid. This delay arose in part because ouabain caused large changes in respiration and blood pressure which interfered with maintenance of the steady-perfusion rates needed for measurement of CSF production by the inulin dilution technique. Perfusion with CSF containing ouabain usually caused hyperventilation and a gradual rise in blood pressure (pressure often exceeded 250 mm Hg). After about 1 hr these effects subsided, rate of cisternal outflow became constant, and steady-state measurements of CSF production rate could be resumed.

**Dependence of potassium outflux on concentration.** Potassium outflux (k_{oua}) was determined as a function of mean CSF potassium concentration in three dogs. Results are shown in Fig. 4A. Over the concentration range, 0.7 mmol/l, potassium outflux was almost a linear function of concentration. When CSF concentration was increased above 10 mmol/l, potassium outflux no longer increased in proportion to concentration. This effect was reversible. The deviation from linearity observed at higher CSF concentrations may indicate that the rate of potassium transport is approaching the maximum capacity of the active transport system.

In three experiments plasma potassium concentration was decreased by infusion of insulin and glucose and increased by infusion of isotonic KCl. Results are shown in Fig. 4B. Outflux was independent of plasma potassium concentration over the entire concentration range, from 2.2 to 7.2 mmol/l.

**Uptake of CSF outflux by brain tissue.** Figure 5 shows uptake of K^{42} and Na^{22} by brain tissue of rats in relation to total uptake from the perfusion fluid (total uptake includes both transependymal outflux and outflux via bulk absorption). After 4 hr of perfusion, brain uptake accounted for approximately two-thirds of total K^{42} outflux, whereas less than 20% of Na^{22} outflux was recovered from brain. However, the uptake by blood (calculated as the difference between total uptake and brain uptake) was approximately the same for the two isotopes. The large difference between the Na and K outflux coefficients (Table 2) can therefore be accounted for by the

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**FIG. 2.** Ionic (Na, K, or Cl) outflux coefficient vs. simultaneous creatinine outflux coefficient. Data are from 12 dogs; brackets indicate that 10^{-6} \text{M} ouabain was added to the perfusion fluid.

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from deterioration of the preparation and illustrates the importance of including a reference substance such as creatinine in studies of ventricular permeability.

**Inhibition of potassium outflux by ouabain.** The large flux coefficients for potassium relative to those for sodium (Table 2) suggest that active transport may account for part of potassium exchange with CSF. Cardiac glycosides inhibit active cation transport in a variety of tissues (5, 17, 22). Effects of adding ouabain to CSF perfusion fluid in one experiment are illustrated in Table 4 and data from five experiments are summarized in Fig. 3. Ouabain decreases the transependymal outflux coefficient of K^{42} from about 0.90 ml/min (at normal creatinine outflux coefficient of 0.25) to about 0.05 ml/min. The residual outflux of potassium after inhibition with ouabain is proportional to creatinine outflux and essentially equal to the sodium and chloride outflux coefficients, as shown in Fig. 2. These results suggest that about 75% of transependymal potassium outflux is dependent on active ion transport.

In contrast to its effect on potassium outflux, ouabain does not change sodium influx significantly. In five dogs treated with ouabain, mean (± SE) k_{Na} was 0.141 ± 0.016 ml/min as compared to 0.154 ± 0.013 ml/min in controls. Because influx continues when outflux is inhibited, potassium concentration of CSF outflow fluid increases. Following addition of ouabain to the perfusion fluid, mean potassium concentration (± SE) of the outflow fluid rose from 3.2 ± 0.1 to 3.8 ± 0.1 mmol/l (N = 6).

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**TABLE 4.** Effects of adding ouabain to CSF perfusion fluid. Data are from five experiments are summarized in Fig. 3, and additional results are shown in Fig. 4. All data are expressed as means ± SE.

<table>
<thead>
<tr>
<th>Ouabain Concentration</th>
<th>K_{oua} (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10^{-6} \text{M}</td>
<td>0.025</td>
</tr>
<tr>
<td>Control</td>
<td>0.05</td>
</tr>
<tr>
<td>Ouabain</td>
<td>0.05</td>
</tr>
</tbody>
</table>
EXCHANGE OF K\(^+\) BETWEEN CSF, PLASMA, AND BRAIN

**TABLE 4. Effects of ouabain on dog 48**

<table>
<thead>
<tr>
<th>Creatinine Outflux Coeff. (k_a), ml/min</th>
<th>(K^{42}) Outflux Coeff. (k_{o2}), ml/min</th>
<th>(K^{39}) Influx Coeff. (k_i), ml/min</th>
<th>(V_i), ml/min</th>
<th>(K_{Conc}) Conc. mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before ouabain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0.03)</td>
<td>(0.193)</td>
<td>(0.182)</td>
<td>(0.043)</td>
<td>(3.4)</td>
</tr>
<tr>
<td>After ouabain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0.037)</td>
<td>(0.079)</td>
<td>(0.165)</td>
<td>(0.004)</td>
<td>(3.4)</td>
</tr>
</tbody>
</table>

relative magnitudes of their respective fluxes from CSF into brain.

Brain tissue of rats normally contains about 100 \(\mu\)Eq potassium and 50 \(\mu\)Eq sodium/g wet wt (10). The total quantity of \(K^{42}\) recovered from brain after 4 hr of perfusion is equivalent to an amount which would be contained in only 0.08 g of brain tissue in equilibrium with the perfusion fluid (2.5 ml CSF containing 3 \(\mu\)Eq potassium/ml would distribute in 0.08 g tissue containing 100 \(\mu\)Eq/g). In contrast to \(K^{42}\), the quantity of \(Na^{22}\) recovered from brain after 4 hr of perfusion is equivalent to an amount which would be contained in 0.7 g, or close to 50\% brain weight (0.23 ml CSF containing 150 \(\mu\)Eq sodium/ml would distribute in 0.7 g tissue containing 50 \(\mu\)Eq/g). Evidently, intracerebral potassium pools act as a sink for \(K^{42}\) outflux, whereas \(Na^{22}\) equilibrates rapidly (within 45 min) with brain tissue close to the CSF. Penetration of \(Na^{22}\) into tissue located farther from the CSF is presumably limited only by the rate of free diffusion through extracellular channels (14).

**Influx of K.** About two-thirds of potassium outflux from CSF is taken up into brain intracellular space (Fig. 5). It can be anticipated, therefore, that potassium entering brain from blood will also exchange with intracellular ion pools. Katzman and Leiderman (11) have shown that more than 40 hr are required for isotopic potassium injected into blood to reach equilibrium (i.e., equal specific activity) with potassium in brain. Therefore, the specific activity (SA) of potassium reaching ventricular perfusion fluid was less than 70\% that in plasma 5 hr after the iv injection of \(K^{42}\), thus indicating exchange with brain potassium. The SA of brain potassium is shown for comparison.

**DISCUSSION**

In this paper it has been shown that the large extraction of \(K^{42}\) fluid perfusing the cerebral ventricles is dependent on uptake of \(K^{42}\) into brain tissue. Approximately two-thirds of the total outflux of \(K^{42}\) was recovered from brain. After perfusion with \(10^{-8}\) M ouabain, the outflux of \(K^{42}\) was reduced to about 25\% of its normal value, indicating that active ion transport is required for the large outflux. The active step in outflux might be ascribed to the ependyma or to cellular components within the brain. Two facts favor the view that the active step inhibited by ouabain is cellular potassium uptake. 1) The fact that relatively large, nonmetabolized organic molecules such as creatinine or even inulin (21) can diffuse across the ependyma makes it unnecessary to assume an active role for ependymal cells. 2) The fact that ouabain does not inhibit transpendymal potassium influx cannot be adequately explained if the active step in outflux is ascribed to the ependyma. Thus if 75\% of normal transpendymal potassium outflux were active,
OUTFLUX

FIG. 4. Effects of potassium concentration on potassium outflux. A. dependence of K⁺ outflux on CSF [K⁺]. K⁺ outflux is expressed relative to outflux at normal CSF [K⁺] (i.e., 3 mmolal). Data are from 3 dogs perfused with CSF of varying [K⁺]. B: lack of effect of plasma [K⁺] on K⁺ outflux. Potassium outflux is expressed relative to outflux at normal plasma concentration (i.e., 4.5 mmolal).

only 25% of outflux would be passive, and it would have to be assumed either that the potassium concentration of brain extracellular fluid is four times that of CSF or that there is a 36-mv potential difference between the two fluids in order to explain the large passive transependymal influx. Both explanations seem extremely unlikely. On the other hand, results obtained with ouabain are easily explained if active transport mechanisms are ascribed to cellular elements of brain. In this case it would be anticipated that potassium influx would not be inhibited by ouabain, for it is well known that ouabain inhibits active cellular potassium uptake whereas potassium outflux from ouabain-poisoned cells is approximately normal (24).

Regulation of CSF [K⁺]. The potassium concentration of mammalian CSF is normally about 2.8 mmolal. Plasma concentration can be varied either acutely or chronically over the range 3–9 mmolal without changing CSF concentration by more than ±0.2 mmolal (2), despite the fact that isotopic potassium exchanges rapidly between the two fluids (7). Specific ion transport systems must exist to account for the observed regulation of CSF potassium concentration. Results presented in this paper relate to the sites of these transport systems.

Ames and associates have observed that the potassium concentration of CSF collected from the choroid plexuses remains close to 3 mmolal when plasma concentration is varied (personal communication), demonstrating choroidal regulatory transport systems for potassium. Figure 6 shows that potassium ions also exchange between CSF and plasma via brain tissue, indicating that there must also be extrachoroidal transport systems for potassium. Transport systems regulating extrachoroidal potassium exchange may be located at the blood-brain barrier or at the ependyma; however, cellular transport systems which maintain high potassium concentrations in brain cells cannot contribute to long term regulation of CSF potassium concentration, since brain potassium content is constant in the steady state. Two facts suggest that the blood-brain barrier rather than the ependyma is the site of regulatory mechanisms. First, Leiderman and Katzman (13) have demonstrated that potassium influx from blood to brain is independent of plasma concentration in rats, indicating that there are regulatory transport mechanisms for potassium located at the blood-brain barrier. Second, as discussed above, the observations that ouabain does not inhibit potassium influx into CSF and that molecules as large as inulin diffuse across the ependyma indicate that transependymal potassium exchange is passive. Present evidence therefore supports the view that two separate ion transport systems are required to explain CSF potassium regulation, one lo-
EXCHANGE OF K+ BETWEEN CSF, PLASMA, AND BRAIN

The exchange of potassium between CSF, plasma, and brain is a complex process involving multiple transport mechanisms. Intraocular injection of K42 revealed a specific activity of influx and brain potassium relative to SA of plasma potassium following injection of K42. Influx data are from 2 dogs and 1 cat. Brain values are from Katzman and Leiderman (11) for rat and rabbit with the exception of the 6-hr point which I determined in a dog.

The high concentration of potassium in CSF (2.8 mmolal) is maintained constant by regulatory transport mechanisms described above. From a functional point of view, it is important to determine whether the concentration of potassium in fluid surrounding neurons within the brain is similar to that of CSF within the large cerebral cavities or whether it is close to that of plasma. The brain is similar to that of CSF within the large cerebral cavities. The potassium concentration of brain extracellular fluid is independent of plasma concentration, indicating that the potassium concentration of brain extracellular fluid is similar to that of CSF with respect to potassium.

A quantitative comparison of transepidermal potassium outflux from CSF into brain with influx from blood to brain indicates that the ependymal linings of the ventricle are much more permeable than the blood-brain barrier to potassium. Therefore, it seems unlikely that substantial concentration gradients of potassium can be maintained between brain extracellular fluid and CSF. Katzman and Leiderman (11) reported an influx of 2.89 mEq/kg per hr into normal adult rat brain, leading to an influx of \(5.3 \times 10^{-4}\) mEq/hr in a typical rat having a brain weight of 1.8 g. The transepidermal outflux coefficient in the present experiments is 0.0148 ml/min (Table 2), leading to a flux of 2.5 \(\times 10^{-4}\) mEq/hr in a typical rat having a CSF potassium concentration of 3. The flux from ventricular CSF to brain is about 50% of that from blood to brain. Since the surface area of the ventricular ependyma is only a small fraction of the brain capillary area, it follows that the permeability of the blood-brain barrier to potassium is extremely small relative to the permeability of the CSF-brain barrier. This result is consistent with qualitative results of Goldmann (6) and many subsequent investigators concerning the relative permeabilities of the two barriers.

Wallace and Brodie have previously suggested that brain extracellular fluid and CSF are in equilibrium (26). They based their conclusion on evidence indicating that the concentrations of thiocyanate, iodide, and bromide in extracellular fluid and CSF are similar, but different from their respective plasma concentrations. Present evidence supports a similar conclusion concerning extracellular fluid potassium concentration. Both the transfemoral potassium influx from CSF to brain (Fig. 4A) and the transcapillary influx from blood to brain measured by Leiderman and Katzman (13) are independent of plasma concentration, indicating that the potassium concentration of brain extracellular fluid is like that of CSF, independent of plasma concentration.

I am indebted to Dr. J. R. Pappenheimer for many helpful suggestions received during the course of the experimental work as well as in the preparation of this manuscript. Thanks are also due Cecile Goodrich, who allowed me to use the apparatus which she had constructed for ventriculo-external perfusion of rats, and James Nicholl for his technical assistance.

REFERENCES


