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Editorial Views

CSF . . . Neural Urine or More?

Many authors envisioned these (CSF) spaces as comprising a microsewage disposal system emptying finally into the subarachnoid cesspool whence the digested residues of neuronal metabolism flowed sluggishly back into the blood stream.[1]

PLUM AND SIESJÖ'S REVIEW of recent advances in cerebrospinal fluid (CSF) physiology demonstrates that the CSF is indeed more than a simple cerebral excrement. As the authors noted, CSF samples from different sites in the central neuraxis reveal chemical concentration differences and provide us with a fluid biopsy representative of the microchemical environment of the brain.

Disease or drug-induced disturbances in the mechanisms regulating CSF composition or its effects can alter ventilation, cerebral blood flow, CSF secretion rates, neuroendocrine relationships, and even affect the maintenance of consciousness. Such alterations are commonly encountered in the practice of anesthesiology. Below, we briefly discuss three areas of current practice and possible future applications of our newly gained insights into CSF physiology. The discussion is directed toward drug effects on CSF secretion rate, modulation of central nervous system functions by CSF electrolytes, and the importance of blood–CSF acid–base relationships in patients with ventilatory alterations.

Drug Effects on CSF Secretion Rate

While it is generally appreciated that anesthetic agents can alter intracranial pressure through their ability to effect changes in intracranial blood volume, there has been, as Plum and Siesjö indicate, no systematic evaluation of the actions of these drugs on CSF secretion rates. Ocular fluid secretion occurs by mechanisms similar to those involved in the formation of CSF, and it has been shown that pentobarbital significantly reduces aqueous humor formation when compared with phencyclidine anesthesia in primates.[2] A similar reduction by pentobarbital of CSF formation rates was found in dogs.[3] This may represent a direct inhibition of specific secretory processes or an indirect retardation of secretion due to blood pressure, cerebral blood flow, or cerebral metabolic actions of pentobarbital. Thus, many commonly employed anesthetics with profound actions on these physiologic functions are likely to alter CSF formation rates.

Under certain circumstances anesthetic effects on CSF formation rates could achieve clinical significance. For instance, a possible reason for the inconsistent results obtained with the CSF–manometric-infusion test for communicating hydrocephalus might be altered CSF secretion rates during the time of the test. Barbiturates or other sedatives could lower the CSF formation rate during the test. On the other hand, a total lack of

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TABLE 1. Selected Normal CSF and Plasma Values*

	$[H^+]$ (nanoEq l)	$[HCO_3^-]$ (mEq l)	P_{CO_2} (torr)	$[Na^+]$ (mEq l)	$[K^+]$ (mEq l)	$[Ca^{++}]$ (mEq l)	$[Mg^{++}]$ (mEq l)	$[Cl^-]$ (mEq l)	Protein (mg 100 ml)	Glucose (mg 100 ml)
CSF	46	23	47	145	2.85	2.45	2.3	113	17–59‡	44–100§
Plasma	38	24	39	139	4.58	4.79	1.8	99	$6–8 \times 10^3$	60–90¶
R_{CSF}†	1.2	0.96	1.2	1.04	0.62	0.51	1.3	1.14	—	—

* Values compiled and averaged from Katzman and Pappius.[5]

† $R_{CSF} = \frac{\text{concentration in CSF}}{\text{concentration in plasma}}$.

‡ Protein content progressively increases from ventricular to lumbar sampling sites.

§ Since CSF glucose levels depend in part on plasma levels, a simultaneous determination of plasma glucose is required.

¶ Fasting blood glucose.

sedation in an excited child or demented patient can also be associated with altered secretion rates. Experiments in unanesthetized monkeys submitted to thermal streses or feeding have shown a uniform depression in the CSF elaboration rate.[4] Clearly, suitably controlled and defined environmental and anesthetic circumstances are required when CSF dynamics are being evaluated.

CSF Electrolytes and Central Nervous System Function

The regional chemical differences (cortical–ventricular–cisternal–lumbar concentration gradients) in CSF are indicative of dynamic processes involving multidirectional interchanges among brain, blood, and CSF. These cerebral transcompartmental interactions normally result in precise regulation of the concentrations of a number of biologically active CSF moieties. Possible mechanisms for the regulation of the CSF components include (a) carrier-mediated ionic transport, (b) active transport against electrochemical gradients, (c) passive migration down such gradients, and (d) sodium–potassium ATPase-activated electrically silent ion pumps, which may cause CSF secretion by osmotically obligated transcellular water flow.[5,6] In this way regulation of the non-acid–base-related CSF solutes resembles that associated with maintenance of CSF proton and bicarbonate levels. The results of these regulatory influences on CSF content are summarized in Table 1. The fact that the ratio of the CSF: plasma concentrations (R_{CSF}) of each solute differs from 1.0 indicates that energy is required to maintain these concentration gradients.

The $[K^+]_{CSF}/[Ca^{++}]_{CSF}$ ratio is known to affect neuronal excitability, and it may be anticipated that changes in this ratio could alter the function of superficially placed nervous system chemoreceptors.[7] There is evidence that changes in this ratio alter the sensitivity of the respiratory medullary chemoreceptors to hydrogen ions.[8] Therefore, interactions between CSF electrolytes and the acid–base solutes ultimately determine ventilatory function, and may even have a similar role in the control of cerebral blood flow. Within certain concentration ranges elevation of the potassium content in tissue microareas causes dilation of the pial vessels.[9] Increased cerebral blood flow and ventilatory rates following seizures might then be due to a combination of CSF hyperkalemia and acidemia.[10] Some of the changes in vital signs occurring during surgery in the posterior fossa may be due to irrigation of chemosensitive areas of the brain stem with fluids not sufficiently similar to native CSF.

CSF electrolytes appear to have a role in the control of body hydration as well. CSF sodium concentration changes with hyper- and hyponatremia. Recent evidence indicates that the level of CSF sodium may have a role in the neuroendocrine response to systemic salt loading.[11] Olsson has shown that sodium receptors located near the third ventricle modulate the dipsogenic, antidiuretic, and

natriuretic effects of intracarotid injections of hypertonic saline solution in goats. His studies cast doubt upon the role of central osmoreceptors in body fluid homeostasis, since ventricular perfusion with equiosmolar hypertonic solutions of urea, fructose, or glycerol had much less effect than did altering the $[Na^+]_{CSF}$.

An anesthetic effect on CSF electrolyte concentrations remains undocumented. Large anesthetic effects on CSF electrolyte composition probably do not occur. When changes in body hydration and hypoxic–ischemic insults are excluded, even severe nervous system diseases do not greatly affect electrolyte concentrations. More likely, anesthetic drugs will be shown to interact with CSF electrolytes at the receptor level or by influencing subsequent neurotransmission.

CSF Acid–Base Regulation and Ventilatory Alterations

The controversy surrounding the mechanisms by which CSF acid–base homeostasis is achieved has been difficult to understand for those not intimately involved in the laboratory solution of this fundamental physiologic problem. However, one need not choose an "active transport" or "passive diffusion" camp in order to gain insight into clinical problems. Chronic acid–base imbalances of a respiratory origin will be reflected in the CSF by a bicarbonate change that amounts to almost 65 per cent of the change in plasma bicarbonate. In chronic metabolic disturbances CSF homeostasis appears better maintained, and CSF bicarbonate will change by only 40 per cent of the blood alteration.[12] If one recalls that the blood-to-CSF gradient for molecular CO_2 is usually quite small, measurement of the arterial blood gases and use of the Henderson-Hasselbalch equation should permit prediction of the CSF *p*H. When the clinical picture deviates from that which might be expected from the calculated CSF *p*H, then actual measurement of CSF acid–base status may be indicated. Although purists generally recommend that only stable state measurements are valid, important clinical trends, which reflect changes in brain metabolism, can be seen in cisternal or ventricular CSF within minutes to hours.[13]

It has been demonstrated that the CSF hydrogen ion concentration during systemic acidosis is inversely related to the patient's level of consciousness.[14,15] This may explain why some patients in respiratory failure with poor CSF acid–base compensation are unconscious, while others with a similar degree of systemic acidosis of a metabolic origin are awake. On the other hand, too-rapid reversal of chronic respiratory acidosis can lead to marked alkaline shifts in the CSF associated with decreased cerebral blood flow, convulsions, and loss of consciousness. The alkaline shift occurs because bicarbonate accumulates in CSF in an attempt to buffer the increased CO_2 levels associated with respiratory failure. When Pa_{CO_2} is reduced by mechanical ventilation, CO_2 clearance from the CSF is rapid while bicarbonate elimination is retarded. Thus the CSF becomes highly alkaline.

Prolonged passive hyperventilation results in a decrease of CSF bicarbonate level. However, the sudden reaccumulation of CO_2 upon cessation of ventilation usually causes no clinically recognized problem if the cause of intracranial hypertension has been successfully treated. The rising plasma P_{CO_2} during the immediate period of post-hyperventilation apnea is rapidly reflected in the CSF due to the high biologic mobility of molecular CO_2. Ventilation will thereby be stimulated, preventing a clinically significant plasma and CSF acidosis. Intact central chemoreceptor function is required for the response to CSF acidification, while peripheral chemoreceptor function provides respiratory stimulation for the few minutes before CSF *p*H decreases significantly.

Following subarachnoid hemorrhage a selective CSF metabolic acidosis can occur due to continued anaerobic metabolism by the erythrocytes extruded into the CSF. This CSF acidosis may contribute to the systemic respiratory alkalosis and altered consciousness seen with subarachnoid bleeding.[16]

Anesthetics may effect CSF acid–base balance by altering cerebral metabolism and blood flow. This effect is important in laboratory studies, while its clinical significance remains unknown. Kjallquist reported less variability in brain and CSF bicarbonate,

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pyruvate, and lactate during experiments with acetazolamide when he changed from pentobarbital to a nitrous oxide relaxant technique.[17] Development of the ventriculocisternal perfusion technique in awake animals for CSF studies has probably precluded the recognition of subtle anesthetic influences on brain–CSF acid–base balance.

Summary

The review of CSF physiology in this issue provides us with a platform from which we can view our emerging understanding of this complex neural secretion. Although we are in an early stage in our understanding of "neural urine," clinically significant information has already been incorporated into practice. In some cases we have useful clinical correlations. In other cases only questions, but some of these promise to be of considerable relevance to the practicing anesthesiologist.

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References

1. Tschirigi RD: Chemical environment of the central nervous system, Handbook of Physiology. Section I: Neurophysiology. Edited by J Field, HW Magoun, VE Hall, American Physiological Society, Washington, D.C., 1960, pp 1865–1890
2. Cevario SJ, Macri FJ: The inhibitory effect of pentobarbital Na on aqueous humor formation. Invest Ophthalmol 13:383–386, 1974
3. Michael DK, Bierer DW, Heisey SR: Effects of anesthesia and hypoxia on cerebrospinal fluid production in the adult dog. Fed Proc 31:395, 1972
4. Meyers RD, Sharpe LG: Cerebrospinal fluid production during temperature stress and feeding in the conscious monkey. Experientia 25:497–498, 1969
5. Katzman R, Pappius HM: Brain Electrolytes and Fluid Metabolism. Baltimore, Williams and Wilkins, 1973
6. Pollay, M: Formation of cerebrospinal fluid. Abstracts of the Second International Symposium on Intracranial Pressure, Lund, Sweden, 1974, A:2
7. Berkenbosch A, Adan AJM: Influence of CSF calcium concentration on the ventilatory response to CO_2 and O_2. Pfluegers Arch 348: 33–50, 1974
8. Berndt J, Berger W, Berger K: Influence of potassium on the respiratory response to changes in CSF *p*H. Resp Physiol 8:177–190, 1970
9. Kuschinsky W, Whal M, Bosse O, et al: Perivascular potassium and *p*H as determinants of local pial arterial diameter in cats: A microapplication study. Circ Res 31:240–247, 1972
10. Meyer JS, Kanda T, Shinohara Y, et al: Changes in cerebrospinal fluid sodium and potassium concentrations during seizure activity. Neurology (Minneap) 20:1179–1184, 1970
11. Olsson K: Further evidence for the importance of CSF Na^+ concentration in central control of fluid balance. Acta Physiol Scand 88: 183–188, 1973
12. Fencl V: Distribution of H^+ and HCO_3^- in cerebral fluids, Ion Homeostasis of the Brain. Edited by BK Siesjö, SC Sorensen. New York, Academic Press, 1971, pp 175–185
13. Salaymeh MT, Geha AS, Baue AE: Value of cerebrospinal fluid as an indicator of cerebral metabolic changes. J Surg Res 11:198–201, 1971
14. Posner JB, Plum F: Spinal fluid *p*H and neurologic symptoms in systemic acidosis. N Engl J Med 277:605–613, 1967
15. Bulger RJ, Schrier RW, Arend WP, et al: Spinal fluid acidosis and the diagnosis of pulmonary encephalopathy. N Engl J Med 274:433–437, 1966
16. Shannon DC, Shore N, Kazemi H: Acid–base balance in hemorrhagic cerebrospinal fluid. Neurology (Minneap) 22:585–589, 1972
17. Kjallquist A, Nardini M, Siesjö BK: The effect of acetazolamide upon tissue concentrations of bicarbonate, lactate and pyruvate in the rat brain. Acta Physiol Scand 77:241–252, 1969

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