# Effects of Hydration on Blood and Cerebrospinal Fluid Osmolalities[1] (34806)

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Bering (1) observed that parenterally administered $D_2O$ moved into the brain parenchyma much more rapidly than into the cerebrospinal fluid. The much greater half-time required for CSF exchange as compared to brain tissue exchange is probably due to the large intercapillary distance and the large distribution volume for the radioactive tracer in the CSF (2). On this basis, we would predict a lag in CSF osmolality changes in response to alterations in blood serum osmolality.

Davson (3) has found the CSF osmolality to be greater than blood osmolality in several laboratory animals; he found this difference to be highly significant ($p < .001$). However, the two fluids appear to be isosmotic in humans (4).

The study reported here was carried out to see if our predictions concerning the relationship of CSF osmolality to changes in blood serum osmolality could be verified and whether Davson's finding that the CSF is hyperosmotic to the blood could be confirmed.

*Methods.* Experiments were performed on 12 cats weighing 1.5 to 3.9 kg. The animals were anesthetized with Nembutal, 40 mg/kg given intraperitoneally. The animals were then immobilized with Flaxedil and were artificially respired at 14–16 per min such that pH and $pCO_2$ were within the normal range. Body temperature was maintained at 37–38° by use of a heating pad. Food and water were withheld for 18 hr prior to the experiment. The femoral vein was cannulated. A cannula was inserted through a lumbar laminectomy and advanced through the subarachnoid space to the region of the cisterna magna. Blood and CSF samples were obtained to serve as baseline values. The animal was then given 10 pressor units of vasopressin intramuscularly. After 30 min, water was infused intragastrically for 1 hr, the animal being given 50 ml of $H_2O$/kg of weight. Once the infusion was ended, blood and CSF samples were obtained for each determination. The osmolality of 0.2 ml aliquots of serum and CSF was determined by freezing-point depression using the Fiske osmometer. In the last nine animals run, Na was determined by internal standard flame photometry and urea nitrogen was determined by the urease method.

*Results.* As indicated in Fig. 1, osmolality of the CSF as measured by the freezing-point depression method with the Fiske osmometer was greater than that of the blood serum in the baseline state. During the course of the hydration, the effect of the administered water load was first revealed as a fall in the serum osmolality. Changes in the CSF osmolality were in the same direction as those of the serum, but always lagged behind them. As a result, the CSF osmolality remained higher than the serum osmolality during the course of the experiment, except at the time of the final determinations when the blood osmolality started to rise but the CSF osmolality remained lower than the blood osmolality due to its characteristic lag.

As can be seen from Fig. 1, the time lag that exists between changes in serum osmolality and changes in CSF osmolality does show variability from animal to animal. We attempted to arrive at quantitative estimates of this time lag by the following arbitrary procedures. The time that was required for the serum osmolality to fall 10 mOsm from its

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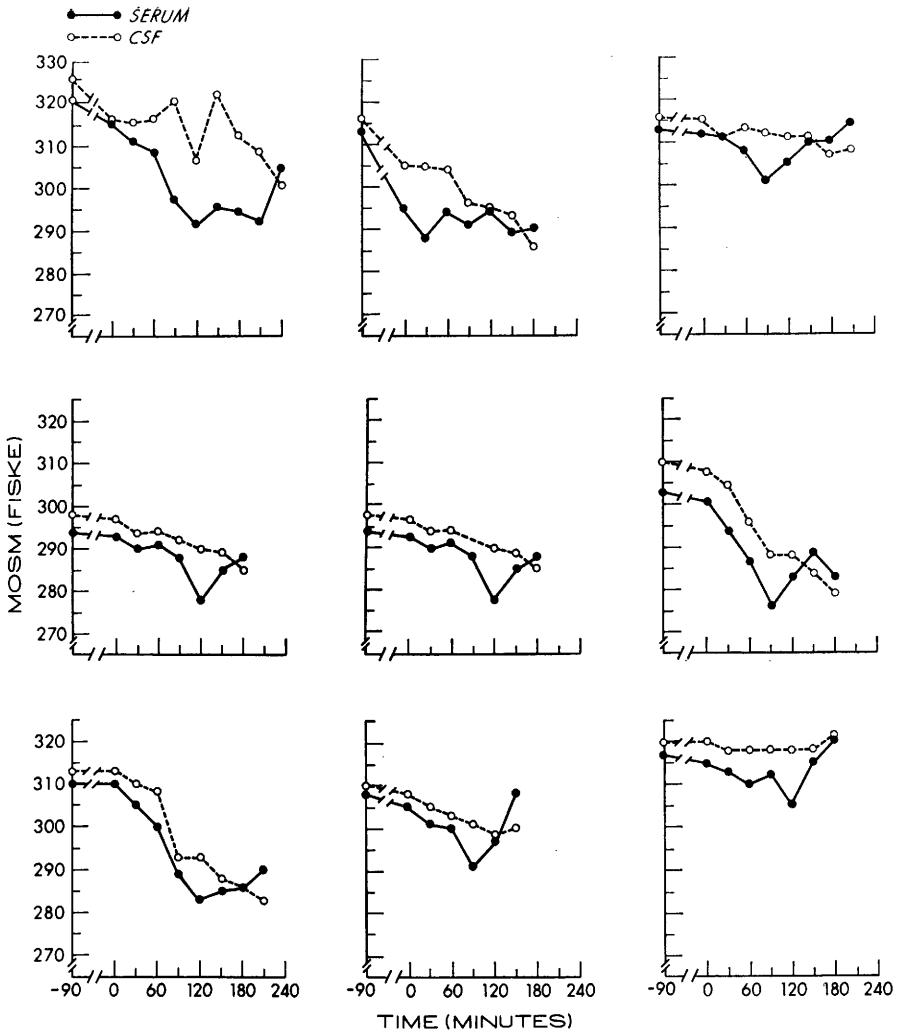


FIG. 1. Time course of CSF and serum osmolality changes during hydration as measured by the Fiske freezing-point depression method. Nine different experiments are illustrated here.

baseline value was noted. This time was then subtracted from the time required for CSF osmolality to fall from its baseline value by 10 mOsm. The resultant time was used as an estimate of the lag time. In our experiments we found a mean lag time of 45 min, with extremes of 15 and 90 min.

It is also possible to estimate the lag time by an alternate approach. The time required for serum osmolality to fall 10 mOsm from its baseline value was subtracted from the time required for CSF osmolality to equal his reduced value of serum osmolality. This method, when applied to our experimental data, yields a mean lag time of 65 min, with extremes of 15 and 105 min.

During the process of hydration, the Na content of the serum fell from an average baseline value of 155 meq/liter to an average level of 140 meq/liter. This was paralleled by a fall in the Na content of the CSF from its average baseline value of 155 meq/liter to an average value of 142 meq/liter. During the hydration process the average urea nitrogen content of the serum rose from 28 to 30 mg/100 ml while that of the CSF dropped from 23 to 20 mg/100 ml but these changes are not statistically significant.

The effective osmotic pressure can be calculated by use of the reflection coefficient of 0.44 for urea obtained from the work of Fenstermacher and Johnson (5). It would be more rigorous to include in the above expression a term to correct for the effect of glucose. However, since the reflection coefficient for glucose is 0.89 (5), we consider it sufficiently close to unity for the purposes of our calculations so as not to warrant a special correction term. The effective osmotic pressure then equals the osmotic pressure as measured by the Fiske freezing-point depression minus (1–0.44) times the urea nitrogen concentration in millimoles:

$$\text{mOsm (eff)} = \text{mOsm (Fiske)} - (1 - 0.44)\frac{(\text{Urea N mg/100ml})}{(2.8)}$$

Implicit in this calculation of effective milliosmolality is the assumption that the reflection coefficient for NaCl is unity, or very nearly so. We feel that this assumption is justified since Davson and Pollay (6) have demonstrated an appreciable blood–brain barrier to $^{24}Na$ (time constant = 0.005 $min^{-1}$). In Fig. 2 we see plotted against time the average effective osmolalities calculated from the CSF and blood serum values obtained from the nine experiments of Fig. 1. It is seen that the effective osmolalities of CSF and blood serum bear the same general relationships to each other as do the freezing-point depression values as measured directly by the Fiske method.

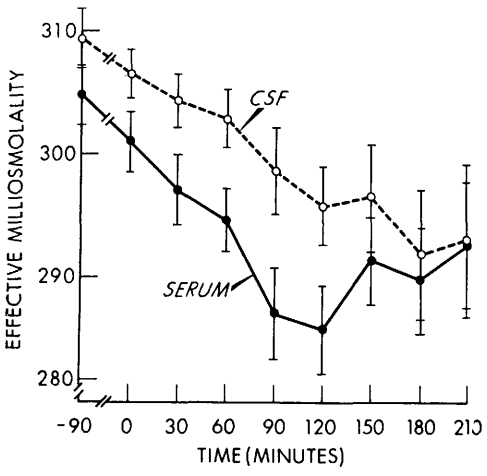


FIG 2. Effective osmolality of CSF and serum as function of time. Each point represents the average of nine independent experiments ± standard error.

*Discussion.* These results confirm our predictions that changes in CSF osmolality lag behind changes in serum osmolality during hydration. This phenomenon may be of significance in clinical situations where there are rapidly occurring changes in blood osmolality.

Flexner (6) has calculated that the total CSF volume of the cat is approximately 4.4 cc. Katzman *et al.* (7) reported that the rate of CSF formation in the cat is 0.016 ml/min or 0.480 ml/30 min. Consequently, in our experiments the withdrawal of 0.25 ml of CSF per half hour would not seem to be an excessive amount of depletion. Moreover, it is clear that any removal of CSF would only tend to reduce the magnitude of the effects that we noted so that under ideal conditions the differences between CSF and serum osmolality would be even more pronounced.

Hypertonicity of CSF with regard to the blood serum has been observed by Davson. We had once thought that this difference might be an artifact due to hydration of experimental animals in the morning leading to greater dilution of blood than CSF. But in our experiments, in which the animals had been dehydrated, this explanation would not be valid. The blood serum would be expected to show the greatest effects of dehydration (*i.e.*, hypertonicity) with relative sparing of CSF tonicity.

The hypertonicity of CSF in these animals may reflect the secretion of a hypertonic CSF. However, it is difficult to accept this possibility when one calculates the osmotic pressure difference that would be produced by this differential in osmolality. In order to convert an osmotic pressure difference of 1 mOsm to a pressure differential expressed in centimeters of $H_2O$, we use the relation

$$\pi = \Delta c R T,$$

where $\pi$ = osmotic pressure expressed in cm $H_2O$,
$\Delta c = 0.001$ moles/liter,
$R = 84.8$ liter cm $H_2O$/mole °K, and
$T = 310$ °K.

$\pi$, then, equals 26.3 cm $H_2O$ for an osmotic pressure difference of 1 mOsm. Thus, the difference between the mean effective osmolality of CSF and serum in the baseline state, *i.e.*, 4.3 mOsm, corresponds to a pressure differential of 113 cm of $H_2O$, a value that exceeds by a factor of 10 the normally existing pressure differentials between blood and CSF.

In interpreting the results of our experiments, one must remain open to the possibility that osmolalities measured on the Fiske instrument via freezing-point depression do not necessarily reflect the osmolality that would be expected at 37°. A small error might well be introduced by the changes in the complexing of molecules that occur at different temperatures. Since spinal fluid contains such a low proportion of organic molecules, it seems most likely that any error produced in these osmolality measurements by the temperature changes occur in blood serum.

*Summary.* The CSF and serum osmolalities have been studied by the Fiske freezing-point depression method in dehydrated cats undergoing rapid hydration. In the initial baseline dehydrated state the CSF is hypertonic to blood by 4.3 mOsm on the average. During hydration the osmolality of both fluids fell but the CSF osmolality changes lagged behind changes in blood osmolality. The lag in CSF osmolality was quite variable but averaged between 45 and 65 min, depending upon the method of estimating it. When blood osmolality started to rise, there was often a transient period of CSF hypotonicity to blood. These findings can be attributed to the large intercapillary distances existing in the CSF compartment as compared to brain.

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