DISTRIBUTION OF INTRACRANIAL CONTENTS
AFTER HYPERTONIC UREA*

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The intracranial contents are distributed among four component units: blood, cerebrospinal fluid, brain water, and brain solids. The relationships of these components may be altered by chemical or physical means, one example of which is the infusion of hypertonic urea. Following the administration of urea, a redistribution in the fluid units is observed which is accompanied by a decline in cerebrospinal-fluid pressure: the volume of brain water decreases and there is an increase in the combined blood and cerebrospinal-fluid volumes. The amount of brain solids remains unchanged, so there is no net loss of total fluid from the head.

Hypertonic solutions were shown to be effective agents for the reduction of intracranial pressure by Weed and his associates more than 40 years ago. During the period following the experiments of these investigators, hypertonic sodium chloride or glucose was employed clinically to lower increased intracranial pressure, but this practice fell into disrepute because of a "rebound" rise in cerebrospinal-fluid pressure once the effect of the hypertonic solution had become dissipated. When the use of hypertonic urea was reintroduced in 1950, it was alleged that rebound did not occur following its administration. However, personal clinical observations and fragmentary experimental evidence suggested that, like the other hypertonic agents, there was a rebound rise in cerebrospinal-fluid pressure associated with the use of urea. In order to verify these findings, the present study was undertaken in which it was demonstrated clearly that a definite, but delayed, rebound phenomenon did follow the infusion of hypertonic urea.

METHODS

The experimental animal was the dog, unselected as to age and sex. The animals were anesthetized with sodium pentobarbital and an endotracheal catheter was inserted. The dogs breathed room air and respirations were spontaneous. Urea was given intravenously in the form of urevert, 6 gm./kg. at 60 drops per min. The method for the simultaneous determination of intracranial contents to be described below was applied to groups of animals 30 min., and 6, 12, 18, and 24 hours after the infusion of the urea. The data for the 30-min. determinations were reported previously.

Cerebrospinal-fluid pressures were measured from a special catheter placed surgically and fixed with a watertight seal into the cisterna magna. The catheter was attached to a water manometer and observations were recorded every 5–10 min. throughout the 24-hour period of the experiment. The dog was in the lateral recumbent position.

The distribution of the intracranial contents was determined in the following manner. One hundred microcuries of radioiodinated serum albumin were given intravenously and 15–30 min. were allowed for the equilibration. Then 10 ml. of blood were removed from the femoral artery, the dog's head was plunged into liquid nitrogen, and cardiac action was stopped by an overdose of sodium pentobarbital injected into the heart. The head and neck were packed in dry ice for 12–24 hours to assure solid freezing of the intracranial

* Urevert is a 30 per cent solution of urea in 10 per cent invert sugar. The Urevert used in these experiments was supplied by the Baxter Laboratories, Morton Grove, Illinois.


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contents. The dog was decapitated and the head was split in the midsagittal plane.

The frozen intracranial contents were removed in the cold room to preserve their solid state. The tissue was divided into two portions. One portion contained 5–10 ml. of tissue from representative sections of all areas of the brain. Care was taken not to include cerebrospinal fluid from the subarachnoid space or ventricles in this sample—Sample B. The remaining brain, together with the intracranial cerebrospinal fluid down to the level at the foramen magnum, was set aside in the second portion. This sample contained also the leptomeninges and blood from the superior sagittal sinus—Sample S.

Both portions were placed in individual glass-metal tissue homogenizers. A measured amount of water was added to each homogenizer. Following homogenization, the contents were transferred to volumetric flasks. Each flask was brought to the volumetric mark with a measured amount of water. The difference between the calibrated volume of the volumetric flask and the amount of water added to the sample and flask represented the volume of intracranial contents in the flask.

The blood, taken at the time of sacrifice, was centrifuged at 3500 RPM for 60 min. to determine the hematocrit. Aliquots of homogenate and plasma from the hematoctew tubes were counted in a well-type scintillation counter. The aliquots of homogenate were returned to their flasks and each flask was weighed to an accuracy of 0.1 gm. The flasks were dried to constant weight in an oven at a temperature of 100–105°C. and then were reweighed. The difference between the weights of the flasks before and after drying was the weight of water lost from the flask. Since 1 gm. of water equals 1 ml. of water, the difference in weight represented the total volume of water in the flask. The following formulae were applied and the volumes of the intracranial compartments were calculated.

Vol. of cranial contents = vol. of flask

\[ \text{Vol. H}_2\text{O} = \text{wt. of full flask} - \text{wt. of dried flask} \]

\[ \%H_2O = \frac{\text{vol. H}_2\text{O}}{\text{vol. cranial contents}} \]

Blood vol. (BV) = \frac{RISA count/ml plasma}{RISA count/ml homogenate \times 200}

\[ \div 100 - \text{hematocrit value} \]

\[ + \text{total intracranial vol.} \]

CSF vol. (CSFV) = \frac{(%H_2O_S - %H_2O_B)}{100 + (100 - \text{vol. S})} \times \frac{100}{100}

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\text{Brain H}_2\text{O} \text{ vol.} = [100 - (\text{CSFV} + \text{BV})]\times \%H_2O_B
\]

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\text{Brain solids vol.} = 100 - [(\text{CSFV} + \text{BV})] \times (100 - \%H_2O_B)
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\text{S.D.} = \sqrt{\frac{\sigma^2}{n}} \quad \text{S.E.} = \frac{\text{S.D.}}{\sqrt{n}}
\]

RESULTS

The data comprising the first portion of this study were reported previously in this Journal. In these experiments, the distribution of the intracranial contents was determined at the lowest point in the curve of the cerebrospinal-fluid pressure following the administration of the hypertonic urea. The average low pressure was –37 mm. of water which was attained 30 min. after completion of the infusion of urea. At this point, the intracranial contents were distributed among: blood 4.97 per cent, cerebrospinal fluid 11.82 per cent, brain water 58.00 per cent, and brain solids 25.21 per cent (Table 1). When compared with the control values, there was no net loss of total fluid from the head (Table 2). Only a redistribution of the fluid had occurred; brain water decreased as blood volume and cerebrospinal-fluid volume increased. The changes were, in their sum:

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\text{Fig. 1. Gains and losses in fluid volumes during and after the infusion of urea expressed as per cent total intracranial volume.}
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