glucose caused an increase of the free and the total water in the brain, while only a slight increase was seen by that of Polytamine or Lans' solution and no increase was observed by plasma.

Increase of brain volume of equal size was produced in cats by such various method as a) ligation of bilateral jugular veins, b) intracarotid injection of distilled water, c) cerebral concussion, d) irrigation on the surface of the brain with physiologic saline solution at the higher temperature between 43°C and 45°C, e) obstruction of the aqueduct.

In case of a), b), and c), the increase of the free and the total water as well as Na and Cl, decrease of K were seen in the cortex, while in case of d), increase of the bound water, and decrease of Na, Cl and K were observed. However, histological and electron-microscopical investigation could not reveal any essential difference between the edema (a, b, c) type and the swelling (d) type. In case of e), no change was seen in water content or electrolyts of the cortex.

E3. Treatment of Brain Edema Especially Urea-Therapy.

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This paper presents our clinical experiment on the pharmacological approach to brain edema. The result of the medication was evaluated in terms of shrinkage of the brain observed on craniotomy and pressure decrease measured by direct drainage of ventricle.

As to the effect of 30% urea solution on intracranial hypertension, it is almost 4 times as potent as 50% glucose, if the dosis of the former is same with that of the latter, and the higher the dosis given per kg. of body weight, the better was the result.

687 cases (221 patients) of urea medication were examined from various angles. Marked shrinkage of the brain bulk was seen in cases for which more than 1.4 gm. urea/kg. body weight was administered, while moderate shrinkage was seen in cases for which less than 1.3 gm. urea/kg. body weight was used. Edema of subtentorial tumor was less sensitive to the urea administration than that of supratentorial tumor.

Shrinkage induced by the urea solution was more prominently seen on the brain without edema than the one with edema. Of a hydrocephalus no definite effect by urea could be foretold. Our experience is that administration of urea solution under hypothermic anesthesia is very potent and it renders a manual procedure in a deep spot of the brain easier.

In a non-craniotomy case, the effects of urea solution were represented as disappearance of symptoms by pressure cone, improved EEG findings and nor-

malized hemodynamics of the cerebral circulation.

Through clinical observations, it was found that urea gives no significant influence on blood pressure, hematocrit, plasma protein, hepatic function, renal function and electrolyte balance.

Distribution and deposit of urea in a body and also rebound phenomenon were discussed, but they deserve further investigations here-after.

Of other agents for intracranial hypertension than urea solution, it was observed that 50% fructose added with aminophyllin or 50% glucose containing aminophyllin is almost as potent as urea.

E4. On the Brain-Edema and the Blood-Brain-Barrier.

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There are many discussions on the definition and the pathological-physiology about so-called brain-edema and -swelling, it, however, is certain that these have direct connection with increase of the brain volume and the water contents of brain tissue. In the point of such signification, we have discussed about next some problems of urea from the therapeutic standpoint.

1) Change of the concentration of urea in the vital body. The mechanism of urea has been stated generally that it is an osmotic pressure due to change of the concentration of urea in the serum and the C.S.F. or it is related to passage in all the barrier. We have recognized the tendency that the serum concentration increases within relatively short time (25-30 minutes in the experimental case and about 60 minutes in the clinical case) after infusion of urea, and the equilibrium of serum- and C.S.F.-concentration is inverted after certain progress. We found that urea-¹⁴C appeared each other in the C.S.F. after venous injection and in the blood after application into the cisterna magna, and also it was proved in the brain tissues itself, especially lesser in white matter than grey matter in radioactivity. When urea was taken under the hypothermia, the appearance-time of maximum concentration in the serum of it, and equilibrium of concentration between serum and C.S.F. were delayed in comparison with normothermia. It seems to be related to rapidity of urea distribution due to slow rate of hemodynamics, and moreover to be displayed increased effect in reduction rate of intracranial pressure and in its maintenance-time.

2) Water contents of brain tissue. When we observed it with infusion of urea, its average rate showed decrease of 20 per cent in 2 hours. From this point, it seems to be considered decrease of volume of brain.

3) Circulating-time of the brain. After administration of urea, it was shown tendency of slight reduction in the normal brain, but markedly improvement in the