It should be pointed out that the rat is highly refractive to the action of crotalin. A rat weighing 150 gm. is not killed by an injection of one-third of the usual lethal dose for a dog weighing 10 kg. A subcutaneous injection of crotalin into the white rat is not followed by sloughing which usually follows subcutaneous injections into dogs and rabbits.

5415

On the Cause of Brain Edema After Pitressin.

H. G. BARBOUR, G. E. ELLERBROOK AND M. W. HOWARD.

From the Department of Physiology and Pharmacology, School of Medicine, University of Louisville, Kentucky.

Brain hydration has been shown[1] to accompany the anuria of rabbits injected with pitressin. We are now attempting by studies of brain swelling, to throw some light upon the cause of this pitressin edema.

In our first experiments, post-mortal swelling of dogs' brains in their own defibrinated blood was studied with and without the addition of pitressin. Pitressin (P. D. & Co.), which contains 0.5% chloretone was added, usually in the ratio of 2 cc. to each 25 cc. of defibrinated blood. In the control experiments, 2 cc. of 0.5% chloretone was added instead. (The brains were all obtained from dogs killed after 2 or 3 hours moderate etherization preceded by morphine.)

In each of 5 animals it was found that both the cerebrum and medulla swelled more slowly and to a less extent in the presence of pitressin. This difference was at first more pronounced in the cerebrum. The average weight increases from three nearly identical experiments for the second hour were: *cerebrum,* normal 7.1%, after pitressin 5.7%; *medulla,* normal 5.0%, after pitressin 4.5%. Four hours post mortem the following increases were noted: *cerebrum,* normal 7.8%, after pitressin 6.8%; *medulla,* normal 5.7%, after pitressin 4.5%.

Rabbits were given water *per os,* 75 cc. per kilo. Each day a rabbit was given, just after the water, ½ cc. pitressin per kilo. After an interval which varied from 15 minutes to one hour, the animals

[1] Ellerbrook, G. E., Dunham, E. S., and Barbour, H. G., *J. Pharmacol. and Exp. Therap.,* 1930, **39**, 249.

were killed by a blow on the head. In the blood of rabbits killed 15 to 30 minutes after pitressin injection, a normal rabbit brain gains considerably less weight than in its own blood. A pitressin rabbit's brain, however, shows in its own blood a normal degree of post mortal swelling. Thus the pitressin rabbit's blood appears to have the capacity to dehydrate a normal brain, just as when pitressin was added to the dog's blood in the *in vitro* experiments cited above. This point was tested on 6 pairs of rabbit cerebra and in 4 of these pairs we also tested the medullae. All these experiments gave the same qualitative result.

In the blood of rabbits killed 15 to 30 minutes after pitressin plus H_2O, normal rabbit brains showed the following respective weight increases during the first 3 hours: 2.5%, 5.0%, 6.6% (average of 6 experiments). The pitressin rabbits' brains in their own blood, gave the following: 4.5%, 6.7%, 8.1% (average of 6 experiments).

In the blood of rabbits killed 15 to 30 minutes after water only, the brains of the same rabbits gave the following: 4.4%, 6.1%, 7.8% (average of 6 experiments).

In 2 experiments in which the pitressin rabbit was killed respectively 45 and 60 minutes after the injection, a different picture was obtained. Here both the normal brain and the pitressin rabbit's brain were considerably *hydrated* by the pitressin rabbit's blood.

In the blood of rabbits killed 45 to 60 minutes after pitressin plus H_2O, normal rabbit brains showed the following respective weight increases during the first 3 hours: 6.7%, 9.2%, 9.5% (average of 2 experiments). The pitressin rabbits' brains, in their own blood, gave the following: 5.6%, 8.7%, 11.1% (average of 2 experiments).

In the blood of rabbits killed 45 to 60 minutes after water only, the brain of the same rabbit gave the following: 4.4%, 6.6%, 8.7% (average of 2 experiments).

The fact that the brain showed increased swelling in these latter cases may perhaps be best explained on the assumption that 45 minutes after injection significant amounts of pitressin will not remain in the blood. In the earlier paper we showed that rabbits given this dose of pitressin usually exhibit marked diuresis for the first half-hour, followed by anuria with brain edema. We find that the procedure described above produces more blood hydration in the pitressin rabbits than in the normals, the blood specific gravity continuing to fall for over one hour. In view of these several facts, we may attribute the later pitressin augmentation of brain swelling

as due to the contact of that organ with an abnormally hydrated blood from which the pitressin has largely disappeared.

Conclusions. 1. Pitressin, added to blood *in vivo* or *in vitro,* diminishes post-mortal swelling of the normal brain. 2. Pitressin probably disappears from the blood within 45 minutes after subcutaneous injection in rabbits, for brain swelling then becomes augmented. The brain edema previously demonstrated seems to result from the blood hydration which in turn is associated with anuria, and as previous experiments have shown, with loss of water from the skin.

5416

Guanidine Content of Blood from Epileptics.

M. M. ELLIS, M. P. NEAL AND T. R. FRAZER.

From the Departments of Physiology and Pathology, Medical School, University of Missouri, and State Hospital No. 1, Fulton, Missouri.

The guanidine content of blood from 18 epileptic men and 16 epileptic women, representing a total of 47 epileptic seizures, was determined by the nitroprusside method of Marston,[1] as modified by Weber,[2] and Major and Weber.[3] These blood samples were drawn near the termination of the seizures, often before the patient had completely recovered consciousness. As all of the epileptic subjects were institutional patients, blood samples from 9 non-epileptic men and 10 non-epileptic women, also inmates of the same institution, were studied by the same method to provide controls against the diet and routine institutional life of the epileptic patients. The blood guanidine data have been summarized in Table I.

From the table the high guanidine content of the blood from these epileptics in seizures is evident. The maximum blood guanidine found in the samples from the non-epileptic cases was 0.48 mg. per 100 cc. of blood, (individual data not presented in detail here), which value was exceeded in 29 of the 47 epileptic cases. The average blood guanidine for the non-epileptics was near 0.2 mg. per 100 cc., which is slightly higher than the average from the non-hypertension cases presented by Major and Weber[3]

[1] Marston, Austral, *J. Exp. Biol. Med. Sci.*, 1924, **1**, 99.

[2] Weber, PROC. SOC. EXP. BIOL. AND MED., 1927, **24**, 712.

[3] Major and Weber, *Arch. Int. Med.*, 1927, **40**, 891.