calcium-high-phosphorus diet. Therefore, even if the material used is contaminated with vitamin D, or in itself has antiricketic properties when used in massive doses, the difference in its action upon the two types of rickets is manifest. Although the exact composition of the preparation is not known, it is obvious that it does not contain a large amount of vitamin D, for it did not cure rickets in rats resulting from high-calcium-low-phosphorus intake, even with the largest doses used. Furthermore, the cure of the rickets in rats resulting from low-calcium-high-phosphorus diets was not effected by the toxic factor, for the blood serum calcium was not raised nor was pathological calcification produced in the soft tissues. It is reasonable to conclude, as do Albright *et al.*, that A.T.10 and vitamin D affect calcium and phosphorus metabolism to a different degree, and that A.T.10 is more effective in preventing rickets induced by the low-calcium-high-phosphorus diet because it facilitates the elimination of phosphate in the urine and hence renders this type of diet less ricketogenic.

Summary. The effect of A.T.10 on prevention of rickets in rats differs according to the ricketogenic diet fed. Rickets caused by high-calcium-low-phosphorus diets was not prevented by a non-toxic amount of A.T.10 which protected rats fed low-calcium-high-phosphorus diets.

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Resistance of Young Dogs to Acute Arrest of the Cephalic Circulation.*†

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The observation has been made by several investigators that the young animal is much less susceptible to asphyxia than the adult.[1, 2]

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1 Reiss, M., *Z. f. d. ges. exp. Med.*, 1931, **79**, 345.

2 Avery, R. C., and Johlin, J. M., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1184.

No information has been available, however, concerning the essential factors involved in the greater resistance of the young to asphyxia. It was of interest, therefore, to determine whether the brain itself is more resistant to anoxia and accumulation of metabolites in the young animal. This question has been investigated by comparing the effects of complete arrest of the cephalic circulation for various periods of time in adult dogs and in puppies. The method which has been employed to produce sudden complete stasis of blood in the head by means of a pressure cuff in the cervical region has been described[3] as has also the effects of this procedure on adult animals.[4]

The adult dog rarely recovers consciousness after 8 minutes of complete vascular occlusion. It remains comatose as long as it lives, losing all sensation and retaining only very primitive responses on the reflex level. After 6 minutes of vascular stasis, consciousness is recovered in 24 to 48 hours as a rule and following this, the animal is very severely ataxic, restoration to normal requiring a period of weeks or months. Following 4 minutes of arrest of the cephalic circulation, consciousness returns in 18 to 24 hours and the residual ataxic symptoms, though somewhat less severe, are still present. After only 2 minutes of vascular occlusion, slight ataxia persists for a week or more.

Complete arrest of the cephalic circulation was produced in 8 puppies using the same technic as had been employed in the study of adult animals. The results of temporary cessation of the brain circulation in these animals are in striking contrast to the effects of the procedure in the adult. Various responses such as the wink reflex, respiration, struggling of the body and movements of the tail all persist longer after arrest of cephalic blood flow in the young animal. Thus the lid wink persisted for one minute and in some cases for 1½ minutes after vascular occlusion in the puppy, while it disappeared in 10 to 20 seconds in the adult. Similarly, gasping continued for 2½ minutes as a rule, while in the adult all respiration had ceased less than one minute after circulatory arrest. Movements of the legs and tail continued for an average of 6 minutes in the puppy, while in the adult, movements had ceased within 2 minutes. However, there is little reason to doubt that the arrest of circulation effected by the procedure is complete, since after an arrest of cephalic circulation for 10 to 12 minutes, the wink reflex did not return for 8 to 10 minutes following restoration of blood flow.

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3 Kabat, Herman, and Dennis, Clarence, PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 864.

4 Dennis, Clarence, and Kabat, Herman, PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 559.

Six of the puppies were littermates, weighing 2 pounds, all of whom were studied on the same day at the age of 45 days. Following 4 minutes of circulatory stasis, a puppy could stand and walk with only moderate ataxia within 20 minutes. After 1½ hours, the animal was quite responsive and could walk without ataxia, and its behavior differed very little from that preceding the arrest of blood flow.

In another animal, 4 hours after complete circulatory arrest of 12 minutes' duration, the puppy was able to stand and walk very ataxically, walking on a broad base with the nose close to the ground. It responded sluggishly to sound and light and was very hyperactive, walking all of the time. After 24 hours, the puppy was unable to stand or even to turn from its side to its belly, although it was able to lap milk, see, and hear. It gradually improved, so that on the third day following the arrest of the cephalic circulation, the animal was able to stand and walk but very ataxically, falling frequently. Much cerebral function was retained, since the puppy responded to petting by wagging its tail, came when he was called and walked across the room for his milk, etc. At 10 days, the chief symptom was a moderately severe ataxia with an intention tremor of the head.

In another animal, 16 minutes of cephalic vascular stasis resulted in coma which persisted. The animal never regained consciousness or sensations and only primitive reflex responses remained.

In order to examine more closely the age factor in the resistance to arrest of the cephalic circulation, 2 littermate puppies were subjected to circulatory arrest of 10 minutes' duration, one at the age of 48 days and the other a month later at the age of 77 days. The younger animal was able to see and hear, stand and crawl forward ataxically 2 hours after the procedure. The next day it showed only a slight ataxia, from which it recovered completely by the second day, at which time its behavior was quite normal.

The older littermate was much more severely affected by the 10 minutes of circulatory arrest in the brain. After 6 hours, it was semi-comatose, gave evidence of ability to see and hear, and was hyperactive, crawling forward very ataxically. On the following day, the puppy could not stand or even turn from its side to its belly and gave no response to sound or light. It lapped when its mouth was placed in milk. After 4 days, sensation had been restored and the puppy could turn from its side to its belly but was unable to stand or walk. On the fifth day, it could stand and walk very ataxically, came when it was called and was curious about its environment. It is interesting to note that in this case as well as in the 12-minute occlusion described above, recovery had proceeded much further within a few hours after resuscitation than on the following day. This may indicate that a secondary depressive factor acts on the neurons some time after the circulatory arrest.

It is evident from these results that the brain of the young dog is much more resistant to arrest of its circulation than is that of the adult dog and this increased resistance appears to bear a reciprocal relation to the age of the animal. The increased resistance of the young brain to circulatory arrest may correlate with a lower oxygen requirement of the neurons, since Himwich, Baker and Fazekas[5] have demonstrated that the oxygen consumption of slices of infant rat brain is much smaller per unit wet weight than that of the adult and Craigie[6] has shown that the infant brain is considerably less vascular than that of the adult.

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Effect of Hypothermia on Cerebral Metabolism.

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We have previously presented data[1] indicating an increased cerebral metabolism during hyperthermia. In this communication are included the changes of cerebral A:V oxygen differences resulting from hypothermia. The recent work of Smith and Fay[2] in which hypothermia has been used for the treatment of cancer lends added significance to this study.

Dogs anesthetized with pentobarbital were packed in ice. Blood samples were collected from the femoral artery and the superior longitudinal sinus at various intervals while the rectal temperature fell from approximately 38°C to 26°C. The blood samples were analyzed for oxygen[3] and glucose.[4] The velocity of the systemic circulation was estimated by the method of Robb and Weiss.[5] Nine dogs have

[5] Himwich, H. E., Baker, Z., and Fazekas, J. F., *Am. J. Physiol.*, 1939, **125**, 601.

[6] Craigie, E. Horne, *J. Comp. Neurol.*, 1925, **39**, 301.

[1] Himwich, H. E., Bowman, K. M., Goldfarb, W., and Fazekas, J. F., *Science*, 1939, **90**.

[2] Smith, L. W., and Fay, T., *J.A.M.A.*, 1939, **113**, 653.

[3] Van Slyke, D. D., and Neill, J. M., *J. Biol. Chem.*, 1924, **61**, 523.

[4] Hagedorn, H. E., and Jensen, B. N., *Biochem. Z.*, 1923, **135**, 46.

[5] Robb, G. P., and Weiss, S., *Am. Heart J.*, 1932-3, **8**, 650.