CXVII. GUANIDINE STUDIES.

III. WATER CONTENT OF CERTAIN TISSUES DURING ACUTE GUANIDINE AND PARATHYROPRIVIA TETANIES.

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WHILE studying the distribution of injected guanidine in the tissues of guanidine tetany rabbits [Ellis, 1928], it was noted that the actual weights of the brains and kidneys from rabbits in acute guanidine tetany exceeded both the weights of these organs from control animals and the predicted weights for normal animals. A similar comparison of the weights of brains and kidneys from parathyroidectomised cats with normals showed the former to be greater than either the normal or predicted normal weights for cat brains and kidneys. In each group the control and experimental animals were quite comparable as regards body weight, and, as they were killed by drawing off the blood as completely as possible from the carotid artery (the organs being removed to

Table I. *Weights of organs (g.) from normal, injected and parathyroidectomised animals.*

Rabbits, average body-weight 1 kg.					
Animal no.	Experimental factor	Condition when killed	Brain	Kidney	Liver
4*	4 hours 30 minutes after injection 5 cc. physiol. saline	Normal	6.31	6.35	47.92
5*	3 hours after injection 0.1 g. guan. hydrochlor.	Acute tetany	12.34	15.00	42.46
3*	1 hour 15 minutes after injection 0.5 g. guan. hydrochlor.	Acute tetany	8.17	7.56	61.80
1*	6 hours 45 minutes after injection 1 g. phenol	Acute tetany	7.92	10.70	73.09
	Predicted weight for 1 kg. rabbit†		5.84	6.07	52.00
Cats, average body-weight, 2 kg.					
16	55 hours after parathyroidectomy	Tetany	29.30	15.20	65.25
17‡	127 hours after parathyroidectomy	Tetany	24.20	17.20	66.00
22‡	79 hours after parathyroidectomy	Tetany	23.95	18.50	50.40
	Predicted weight for 2 kg. cat‡		20.80	7.40	59.20

* Protocols given in preceding paper.

† Computed from tables of Skelton [1927].

‡ Tetany had been controlled previous to final tetany by injections, as compared with 16 which was uncontrolled.

sealed weighing vessels immediately after the blood was drained off), residual blood in the organs was not a disturbing factor. It was found by checking the gross weights, dry weights and ash, that the extra weight of the brains and kidneys from the tetany animals was due to the greater water content of these organs, and as may be seen in Table I the excess water amounted to 20 % or more.

Table II. *Water content of striated muscle from normal, injected and parathyroidectomised animals.*

Frogs, average body-weight 25 g.			Muscle			
Animal no.	Experimental factor	Condition when killed	Sample	Water %	Solid %	Ash %
7	Normal, 4 hours 15 minutes†	Normal	A	78.78	21.22	—
8	Normal, 6 hours 15 minutes†	Normal	A	79.35	20.65	—
2	3 hours 45 minutes after 30 mg. guan. carb.	Acute tetany	A	81.29	18.71	—
5	3 hours 45 minutes after 30 mg. guan. hydrochlor.	Acute tetany	A	81.51	18.49	—
4	5 hours after 15 mg. guan. carb.	Acute tetany	A	82.48	17.52	—
1	5 hours 30 minutes after 15 mg. guan. hydrochlor.	Acute tetany	A	80.98	19.02	—
6	5 hours 45 minutes after 0.2 g. guan. dextrose	Acute tetany	A	81.49	18.51	—
15	3 hours 15 minutes after 0.4 g. dextrose and 10 mg. guan. carb.	No tetany, sugar-poisoned	A	77.57	22.43	—
Rabbits, average body-weight 1 kg.						
4	4 hours 30 minutes after 5 cc. physiol. saline	Normal	B	78.81	21.19	5.43
5	3 hours after 0.1 g. guan. hydrochlor.	Acute tetany	B	86.11	13.89	5.47
2	1 hour 15 minutes after 0.5 g. guan. hydrochlor.	Acute tetany	B	80.49	19.51	5.96
1	6 hours 45 minutes after 1 g. phenol	Acute tetany	B	77.59	22.41	5.34
Rats, average body-weight 245 g.						
1	Normal; 5 hours 45 minutes after 2 cc. distilled water	Normal	A	73.09	26.91	—
			B	73.07	26.93	4.70
2	5 hours 45 minutes after 0.325 g. guan. hydrochlor.	Tetany	A	74.69	25.31	—
			B	75.45	24.55	4.58
5	1 hour 30 minutes after 0.275 g. guan. hydrochlor.	Tetany	A	76.05	24.95	—
			B	74.95	26.05	4.35
6	8 hours 15 minutes after 0.225 g. guan. hydrochlor.	Tetany	A	81.27	18.73	—
			B	75.55	24.45	—
Cats, average body-weight 2 kg.						
16	55 hours after parathyroidectomy	Tetany	B	78.62	21.38	—
17*	127 hours after parathyroidectomy	Tetany	B	77.84	22.16	—
22*	79 hours after parathyroidectomy	Tetany	B	78.51	21.49	—
25	Normal, control	Control	B	76.14	23.86	—

A Gastrocnemius muscle.

B Leg muscles collectively.

* Tetany controlled by injections previous to final tetany.

† Uninjected animals kept for the time stated under the same conditions as the injected animals, as a control for the water loss by the animal as a whole.

To ascertain more exactly the extent of this change in water content the percentage values for water and solids, and in some cases the ratio of ash to solids, were determined for blood and striated muscles from normal, injected and parathyroidectomised animals.

Table II shows that the water content, compared with the normals, was higher and the total solids lower in the muscle from all tetany animals in which the tetany was induced by guanidine injections or parathyroidectomy. The ratio of ash to solids however was practically the same for both control and experimental animals, indicating that the change in the water-solids ratio in the tetany animals was due to an increase in the water content rather than to a loss of salts. The extra water taken up by the brain, kidneys and muscles during the guanidine tetany could have come from any of several sources including the blood, and the series of water-solids determinations, although small, for blood from three of the rats used (Table III), indicates that the blood is concerned, for the percentages of water were lower and of solids higher in the bloods of the tetany animals than in the normal.

The changes in the water-solids ratio in certain tissues during acute guanidine and parathyroprivia tetanies, particularly the rise in the water content of the muscles and the fall in the water content of the blood in guanidine tetany, suggest that calcium salts, which are known to reduce both guanidine and parathyroprivia tetanies [Fühner, 1906; György and Vollmer, 1922], may effect their action in part by withdrawing water from the muscles. Skelton [1927] found that the administration of calcium chloride to normal animals decreased the water content of the muscles and increased that of the blood. Such action by calcium salts would at least tend to restore the water balance in animals with guanidine and parathyroprivia tetanies and might afford opportunity for the movement of various substances along with the water withdrawn from the muscles.

Whether the increase in water content of these tissues during guanidine and parathyroprivia tetanies was one of the causes of the tetany or whether it was merely a corollary of the tetany was not determined. The muscles from frog No. 15 in which the guanidine tetany was intentionally prevented by an injection of dextrose, and those from the phenol-tetany rabbit did not show a rise in water content. There also seemed to be an indication that the increase in water content of the muscles during guanidine tetany was to some extent correlated with the severity and duration of the tetany. These observations collectively favour the view that the change in water content follows the tetany.

Table III. *Water content (%) of blood from rats listed in Table II.*

Rat no.	Sample 1	Sample 2	Average	Condition of animal when killed
1	81.20	81.80	81.50	Normal
2	75.97	77.80	76.88	Tetany
5	78.13	75.32	76.72	Tetany

In connection with the analytical procedure it should be noted that the changes in the water-solids ratio found in tissues from animals in guanidine and parathyroprivia tetanies have a bearing on the determination of blood- and tissue-guanidines; for the ratio of guanidine to tissue solids in those tissues which took up water, *i.e.* muscle, brain and kidney, would be higher than that derived from the values based on the weight of the normal tissues, while on the same basis the blood-guanidine in terms of normal blood would be too high. Corrections for the water content of the tissues however were not made in the preceding paper as the physiological significance of the excess water was not determined.

SUMMARY.

1. Brain, kidney and striated muscle from animals in acute guanidine and parathyroprivia tetanies were found to have higher water contents than the same tissues from normal control animals.

2. The ash-solids ratio was practically the same for muscle from the tetany animals and from the control normals, showing that the increase in weight of the tetany tissues was due to an actual increase in the water present rather than to a loss of salts.

3. Blood from rats in acute guanidine tetany was found to have a lower water content than normal rat blood.

REFERENCES.

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