CXCII. GUANIDINE AND THE PARATHYROID GLANDS.

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PATON [1916] propounded the theory that parathyroid tetany was due to the accumulation of guanidine in the body on the grounds (1) that the symptoms of tetany could be produced by the injection of guanidine salts and (2) that there was an increased amount of guanidine in the blood stream and in the urine during tetany. Within a few years the theory fell into disfavour chiefly because of criticisms of the chemical methods used [Greenwald, 1919; White, 1927].

The present experiments were carried out to find whether guanidine is present in increased amounts in the blood of dogs in tetany following parathyroidectomy, the method of isolation being one against which such criticisms could not be levelled. [Saunders, 1932].

EXPERIMENTAL.

(1) *Blood from parathyroidectomised animals.*

Four dogs and three cats were bled directly from the carotid artery while in tetany following parathyroidectomy. The blood so procured was extracted for guanidine, but no guanidine was obtained.

Because of the very small amounts of guanidine originally found by Burns and Sharpe [1916] and the lack of delicacy of the method used, these negative results could not be regarded as conclusive.

An attempt was therefore made to find if guanidine is removed from the blood stream of a normal dog at a greater rate than from the blood of a dog in parathyroid tetany.

(2) *Blood from parathyroidectomised animals injected with guanidine.*

Five dogs, all in tetany after parathyroidectomy, were intravenously injected with guanidine solutions so as to give a concentration of guanidine base of 90 mg. per 100 ml. blood, this dose being the same as that used for the normal dogs previously reported [Saunders, 1934]. Each animal was bled as completely as possible at a certain time after the injection, and the blood so obtained extracted for guanidine. The amounts of guanidine recovered were 2.6, 4.1 and 4.5 mg. per 100 ml. blood when the animals were bled 7 min. after the injection, and a trace and 1.7 mg. per 100 ml. blood from two animals bled after 15 min. With normal animals bled 3–7 min. after injection 1.8–4.6 mg. per 100 ml. blood were recovered, a trace after 10 and 14 min., and none after 15 min.

The amounts found are thus substantially the same as those for normal animals. If after parathyroidectomy the mechanism for destruction of guanidine has been removed [Paton, 1924], then after the injection of a relatively large dose of guanidine it should be possible to isolate much more of the guanidine injected.

If on the other hand parathyroidectomy has resulted in guanidine being produced at an increased rate [Paton, 1924] such that even with the normally efficient mechanism for its removal [Saunders, 1934] guanidine is present in the blood stream at a concentration of 1–2 mg. per 100 ml. [Burns and Sharpe, 1916], then the injection of a relatively large dose of guanidine should again result in a large increase in blood guanidine for some time after the injection.

The present experiments show that after the injection of amounts of guanidine which should give 90 mg. per 100 ml. blood, there is no appreciable difference between the amounts found in the blood stream of normal dogs and the amounts found in the blood stream of dogs in tetany following parathyroidectomy. It is therefore improbable that the parathyroid glands regulate the production or destruction of guanidine.

The effects of the injection of guanidine on the blood pressure and heart rate after parathyroidectomy were slight and variable, differing from those of injection into normal dogs. The amounts of blood obtained on bleeding from the carotid artery were 32–35 ml. per kg. in three cases and 53 ml. per kg. in two cases, these being similar to the values from normal dogs.

The methods and experimental details are identical with those given in the previous paper [1934]. The picrates were recrystallised from water and identified by microscopical appearance, M.P., base-N and picric acid content. The figures were (1) M.P. 321°; (2) base-N 15.0 %, picric acid 79.2 %, M.P. 322°; (3) base-N 14.3 %, picric acid 80.1 %; (5) M.P. 326°. Guanidine picrate has M.P. 317–323°, base-N 14.8 %, picric acid 79.5 %.

SUMMARY.

1. No guanidine could be isolated from the blood of animals in tetany after parathyroidectomy.
2. Injected guanidine is removed as quickly from the blood stream of dogs in tetany as from the blood stream of normal dogs.
3. The evidence produced indicates that it is improbable that parathyroid glands regulate either the production or destruction of guanidine.

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