

and inactive animals. However, differences in activity comparable to those in the above groups are accompanied by significant differences in muscle hemoglobin. This is in accord with the observation of Whipple² upon the differences in concentration of muscle pigment in dogs of different breeds and habits.

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Attempts to Demonstrate Vasopressor Properties in the Serum of Hypertensive Dogs.

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Several workers have reported that partial occlusion of the renal artery leads to the accumulation of a pressor substance in the ischemic kidney which may be demonstrated in suitable prepared extracts of the organ.¹⁻⁴ The inference that this substance (renin) is liberated into the circulation with consequent peripheral vasoconstricting action has led to attempts to show that the blood of subjects with ischemic kidneys and hypertension has excessive pressor properties compared to blood from normal subjects. Various test objects have been employed in 2 general methods of approach, (a) injection or perfusion of extracts of blood of hypertensive subjects, and (b) injection, perfusion or cross-circulation of whole blood or serum from hypertensive subjects. By the latter and most significant approach, contradictory results have been obtained.⁵⁻¹²

¹ Harrison, T. R., Blalock, A., and Mason, M. F., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 38.

² Harrison, T. R., Blalock, A., Mason, M. F., and Williams, J. R., Jr., *Arch. Int. Med.*, 1937, **60**, 1058.

³ Prinzmetal, M., and Friedman, B., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 122.

⁴ Govaerts, P., and Dicker, E., *Compt. rend. Soc. biol.*, 1936, **122**, 809.

⁵ Prinzmetal M., Friedman, B., and Rosenthal, N., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 545.

⁶ Prinzmetal, M., Friedman, B., and Rosenthal, N., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 543.

⁷ Collins, D. A., and Hoffbauer, F. W., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **35**, 539.

⁸ Dicker, E., *Compt. rend. Soc. biol.*, 1936, **122**, 476.

Recently Fasciolo, Houssay and Taquini¹² have described a method by which they state that blood taken from the renal vein of an ischemic dog kidney was shown to have increased vasoconstricting properties compared to blood which has passed through a normal kidney. They perfused a L awen-Trendelenberg preparation¹³ of the South American toad (*Bufo arenarum* Hensel) with serum which had been diluted to 8 volumes with Ringer solution, and which contained a final concentration of 0.5% sodium citrate. The blood was drawn directly from the renal veins of normal and hypertensive dogs under chloralose anesthesia. The hypertension had been produced by the procedure of Goldblatt, *et al.*¹⁴ The perfusion rate diminished when the diluted sera of blood from the renal veins of hypertensive dogs was substituted for Ringer's solution to a much greater degree than when the diluted renal venous sera from normal dogs was employed. The vasoconstricting action would gradually disappear when Ringer was again perfused. We have attempted to confirm these important observations.

Experimental. The procedure employed differed from that of Fasciolo, Houssay and Taquini in that the test objects were frogs, bullfrogs and toads from the southern part of the U. S., and the blood for perfusion was withdrawn from the renal veins of unanesthetized dogs with explanted kidneys.¹⁵ In addition the rate of perfusion in the frog was calculated by noting the time required for delivery of unit volumes of 5 or 10 cc of perfusate rather than by drop recording. In other respects the description of their technic was essentially followed. After 5 to 30 minutes perfusion with Ringer, "normal" diluted serum was substituted for 10 to 30 minutes followed by a short perfusion with Ringer, after which the "hypertensive" serum was substituted. This order was, of course, suitably varied.

The results of 26 experiments are summarized in Table I. There was no consistent difference in the effects of "normal" and "hypertensive" sera.

⁹ Heymans, C., and Bouckaert, J. J., *Proc. Soc. Exp. Biol. and Med.*, 1938, **39**, 94.

¹⁰ Houssay, B. A., and Taquini, A. C., *Rev. Soc. Argent. Biol.*, 1938, **14**, 5.

¹¹ Houssay, B. A., and Taquini, A. C., *Rev. Soc. Argent. Biol.*, 1938, **14**, 86

¹² Fasciolo, J. C., Houssay, B. A., and Taquini, A. C., *J. Physiol.*, 1938, **94**, 281.

¹³ Aberdalden, *Handbuch der Biologischen Arbeits-Methoden*, Abt IV, Teil 7B, p. 1754.

¹⁴ Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W., *J. Exp. Med.*, 1934, **59**, 347.

¹⁵ Rhoads, C. P., *Am. J. Physiol.*, 1934, **109**, 324.

TABLE I.
Test Objects: Bullfrogs 16, Frogs 8, Toads 2.

| Alterations in Perfusion Rate Upon Changing Perfusate from: (the numbers refer to the times a given response was observed) | | | | | | | | | | | | | | | | | |
|---|---|----|------------------------------|---|---|------------------------------|---|---|------------------------------|---|---|------------------------------|---|---|------------------------|---|---|
| Ringer to Normal Serum | | | Ringer to Hypertensive Serum | | | Normal to Hypertensive Serum | | | Hypertensive to Normal Serum | | | Hypertensive Serum to Ringer | | | Normal Serum to Ringer | | |
| — | + | 0 | — | + | 0 | — | + | 0 | — | + | 0 | — | + | 0 | — | + | 0 |
| 4 | 7 | 10 | 1 | 3 | 7 | 5 | 2 | 3 | 6 | 1 | 2 | 3 | 0 | 3 | 5 | 0 | 4 |

In a series of 15 additional experiments several variations in technic were introduced. These included, (a) substitution of mammalian Ringer for frog Ringer, (b) elimination of citrate by employing heparin as an anti-coagulant, (c) addition of chloralose to the perfusion fluids and (d) equilibration of the perfusion fluids with O₂—5% CO₂ gas mixture. The results were not significantly different from those shown in Table I.

In our experience the Låwen-Trendelenberg preparation was not a very satisfactory means of studying the vascular effects of dog sera when southern frogs, bullfrogs and toads were employed as test objects. Large spontaneous variations in perfusion rate were encountered with Ringer's solution alone, the rate, on the whole, tending to gradually fall. Substitution of the diluted sera brought about either an increase, decrease or no change of rate. Irrespective of which sera were employed, the rate, after a variable period, would rapidly decrease, the extremities of the preparation would become edematous, and the flow would cease. Return to Ringer except in the early stages would not restore the original rate. The effects recorded in Table I are those occurring during the first part of each experiment before the alterations in rate had become irreversible.

From these experiments we conclude that no particular pressor properties may be demonstrated in the renal venous serum of dogs with hypertension produced by partial constriction of the renal artery when the Låwen-Trendelenberg perfusion technic is employed with southern frogs, bullfrogs, and toads as test objects. The perfusion rate initially may be either increased or decreased by both "normal" and "hypertensive" serum. With prolonged perfusion both types of sera usually cause a profound decline or cessation of flow.

It is to be emphasized that the experiments of Fasciolo, Houssay and Taquini were performed with South American toads whose vascular responses may be different.

Summary. Particular pressor properties could not be demonstrated in serum of the renal venous blood of hypertensive dogs by use of the Låwen-Trendelenberg perfusion technic with bullfrogs, frogs, and toads as test objects.