K". There were no differences observed in the clinical and microscopic picture of the paralytic chicks on the deficiency diet alone or with excess levels of "vitamin K." The effects of high levels of "vitamin K" with experimental rations will be reported later.

Conclusion. Encephalomalacia of chicks is not prevented by the administration of a "vitamin K" excess.

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Effect of Normal and Renal Hypertensive Dog Plasmas on Surviving Arterial Rings.*

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At the present time there is inconclusive evidence both for and against the presence of a pathogenetic pressor substance in the blood of dogs rendered hypertensive by the technic of Goldblatt. We have studied this question by determining the effect of citrated plasmas from normal and renal hypertensive dogs on the tonus of surviving beef arterial rings. Since citrated plasma from normal dogs contains a constrictor substance or substances, we looked for a possible quantitative difference between the tone-augmenting effects of the normal and hypertensive plasmas on the arterial rings.

The method employed was essentially that of Meyer[1] and Dale and Laidlaw.[2] Rings about 4 mm in diameter and 3 mm in width were obtained from the tertiary division of the superior mesenteric artery of freshly slaughtered beeves and stored for 24 to 72 hours in Locke's solution at 4°C. The arterial ring was then placed in a smooth muscle chamber of 8 cc capacity containing oxygenated Locke's solution maintained at 37°C by a constant temperature bath. The lever used magnified the tonus changes of the arterial ring eleven times. The initial tonus of the arterial segment was partially overcome by a stretching load of 2 g attached to the long arm of the lever at the same distance from the fulcrum as the attachment of the artery to the short arm. After the tonus level of the arterial ring had relaxed to an equilibrium level, usually in a period of one hour,

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1 Meyer, O. B., *Z. f. Biol.*, 1906, **48**, 352.

2 Dale, H. H., and Laidlaw, P. P., *J. Pharm. and Exp. Therap.*, 1912, **4**, 75.

the preparation was ready for use, the 2 g weight being used as a lifting load.

The citrated plasmas were obtained from the femoral artery by mixing 1.5 cc of 5% sodium citrate with 18.5 cc of blood. Usually the plasmas were tested only on the same day although on 4 occasions they were again tested after 24 or 48 hours in the ice box at 4°C. Sixteen separate experiments were performed using arterial segments from a corresponding number of beeves. Two normal and 2 hypertensive plasmas were usually employed for each experiment. The suitability of the arterial ring for use was first demonstrated by its prompt vasoconstrictor response to a 1:5,000,000 solution of epinephrine HCl in Locke's solution. Five minutes later, the epinephrine solution was replaced, after washing, by Locke's solution with a resulting return of the ring to its original tonus level during the next 15 minutes. Subsequently the same procedure was used for the plasmas, alternating the normal and hypertensive plasmas. The plasmas were then retested in the same order and finally the epinephrine solution was repeated.

The plasmas from 6 normal and 6 renal hypertensive dogs were tested a total of 3 to 6 times at biweekly or monthly intervals. The plasmas of 3 of the hypertensive dogs were tested both before and after the production of renal hypertension by constriction of the renal arteries.

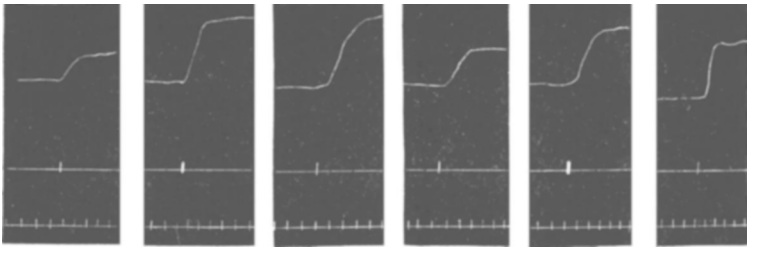
One-third of the relaxed arterial rings showed spontaneous rhythmic tonus changes in Locke's solution which have already been described.[3, 4] Fig. 1 illustrates a typical experiment with 2 normal and 2 hypertensive plasmas. The first normal plasma from a dog with a mean femoral blood pressure (measured by the method of Dameshek and Loman[5]) of 134 mm of Hg. produced an elevation of 21 mm in the writing point of the lever; the first hypertensive plasma from a dog with a blood pressure of 176 mm showed a rise of 23 mm; the second normal plasma from a dog with a pressure of 138 mm caused an increase of 12 mm; and the second hypertensive plasma from a dog with a pressure of 192 mm resulted in an increase of 18 mm. Immediate retesting of these plasmas on the same arterial ring showed the same relationships in vasoconstrictor effect, although the effect was reduced by about one-fourth in each case, undoubtedly due to the removal of some of the vasoconstrictor activity by the arterial ring. This reduction was an invariable finding in all of

[3] Janeway, T. C., Richardson, H. B., and Park, E. A., *Arch. Int. Med.*, 1918, **21**, 565.

[4] Wakerlin, G. E., and Bruner, H. D., *Arch. Int. Med.*, 1933, **52**, 57.

[5] Dameshek, W., and Loman, J., *Am. J. Physiol.*, 1932, **101**, 140.

Figure 1.
The effect of epinephrine and of normal and hypertensive plasmas on the beef arterial ring



1:5,000,000 epinephrine in Locke's solution | Plasma from normal dog with mean b.p. of 134 mm. | Plasma from hypertensive dog with mean b.p. of 176 mm. | Plasma from normal dog with mean b.p. of 138 mm. | Plasma from hypertensive dog with mean b.p. of 192 mm. | 1:5,000,000 epinephrine in Locke's solution

the experiments. The 1:5,000,000 solution of epinephrine produced a rise of 9 mm at the beginning of the experiment and a rise of 18 mm at the end. This increase in epinephrine effect after the plasmas was observed in each experiment and is probably ascribable to the sensitizing action of the plasma proteins.[6]

Subsequent comparisons of the plasmas from these 4 dogs yielded similar results. We were likewise unable to find any correlation between the tone-augmenting action of the plasmas and the blood pressure levels of the other 4 normal and 4 hypertensive dogs. Furthermore, there were no significant differences between the vasoconstrictor effects of the plasmas before and after the production of hypertension in the 3 dogs so studied. The detailed results are illus-

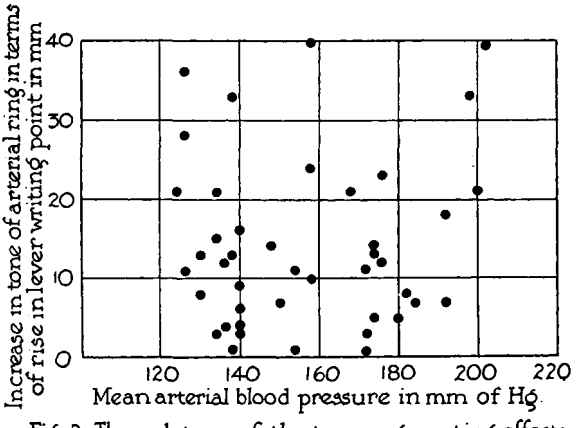


Fig. 2. The relation of the tone-augmenting effects of the plasmas of normal and hypertensive dogs to their mean femoral blood pressure

[6] Freund, H., and Gottlieb, R., *Arch. exp. Path. u. Pharm.*, 1922, **93**, 92.

trated in Fig. 2, where the increases in tone of the arterial rings as measured by the rise of the lever writing point are plotted against the mean femoral blood pressures.

In the 4 experiments where the plasmas were again tested after 24 or 48 hours at 4°C, the vasoconstrictor activity of the plasmas was invariably somewhat more than doubled.

The absence of significant differences in the tone-augmenting property of the normal and hypertensive plasmas for the arterial rings is in agreement with the inability of Page,[7] Collins and Hoffbauer,[8] Prinzmetal, *et al.*,[9] and Heymans and Bouckaert[10] to demonstrate any increase in pressor substances in the blood of renal hypertensive dogs. On the other hand, the reports of Dicker,[11] Govaerts and Dicker,[12] and particularly Fasciolo, *et al.*,[13] suggest a significant increase in the pressor action of the blood of renal hypertensive dogs. The limitations of our method are such that positive results only would be conclusive. The most obvious shortcomings of the method employed are the following: The effects of citrated dog plasma on beef arterial rings *in vitro* are not necessarily analogous to the action of normal plasma on arterioles *in vivo*. The use of dog plasmas and beef arterial rings introduced an unknown factor of species difference. Furthermore, the effect of the possible pathogenetic pressor substance may have been overshadowed by the action of the vasoconstrictor substance present in citrated plasma. And lastly, the hypothetical pressor substance may be present in demonstrable quantities in the venous return from the ischemic kidney but not in the systemic blood. Our results, therefore, by no means rule out the possibility of such a pressor substance in experimental renal hypertension.

Conclusions. 1. The effects of citrated blood plasmas from 6 normal and 6 renal hypertensive dogs on the tonus of arterial segments from the mesenteric arteries of beeves were studied. 2. No significant differences were found in the vasoconstricting properties of the normal and hypertensive plasmas. 3. These results speak against the presence of a peripherally acting pathogenetic pressor substance in the blood of Goldblatt dogs but by no means rule out this possibility.

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7 Page, I. H., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 112.

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

9 Prinzmetal, M., Friedman, B., and Oppenheimer, E. T., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 493.

10 Heymans, C., and Bouckaert, J. J., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 94.

11 Dicker, E., *Comp. rend. Soc. de biol.*, 1936, **122**, 476.

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

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