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Antipressor Effect of Normal Blood in Experimental Hypertension.

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Goldblatt, Lynch, Hanzal and Summerville[1] devised a successful method for producing permanent hypertension by clamping renal arteries in dogs. Many substances like the nitrites and thiocyanates have been used from time to time to reduce blood pressure in man and animals. Extracts of various tissues have been tried also, but none of these have proven to be physiologically specific for hypertension. Experiments are devised in this study to investigate an antipressor substance in blood of normal dogs in relationship to the hypertension of Goldblatt, *et al.*

Method. Initial blood pressures were taken on all dogs without anesthesia by puncture of the femoral arteries. Hypertensive dogs were prepared by the Goldblatt method. Transfusions were made by drawing blood from the femoral arteries of the donors into warm syringes of 100 cc capacity containing sodium citrate solution and injecting it immediately into the prepared foreleg veins of the recipients. Blood pressures were recorded on a kymograph using a cannula between the femoral artery and a mercury manometer. In several experiments the donors' blood pressures were recorded also by the same method. Experiments were carried out using sodium pentobarbital anesthesia. Dogs were used only once.

Results. Two kinds of curves were obtained having distinctly different characteristics (Graph 1). Besides the experimentally produced reduction in the pressure, precipitous falls occurred frequently during the period of transfusion and recovered immediately regardless of the type of experiment or subsequent course of the blood pressure. Donor and recipient bloods were cross-matched and usually showed weak clumping but no true agglutination. Both serum and plasma were used in the cross-matching. No correlation was observed between the results of cross-matching and the type or incidence of pressure changes occurring as a result of transfusion. Such blood pressure changes always occurred within the period of transfusion and the baseline was regained immediately afterwards. The falls were precipitous and occasionally reached shock levels.

[1] Goldblatt, Harry, Lynch, James, Hanzal, R. F., and Summerville, W. W., *J. Exp. Med.*, 1934, **59**, 347.

GRAPH I

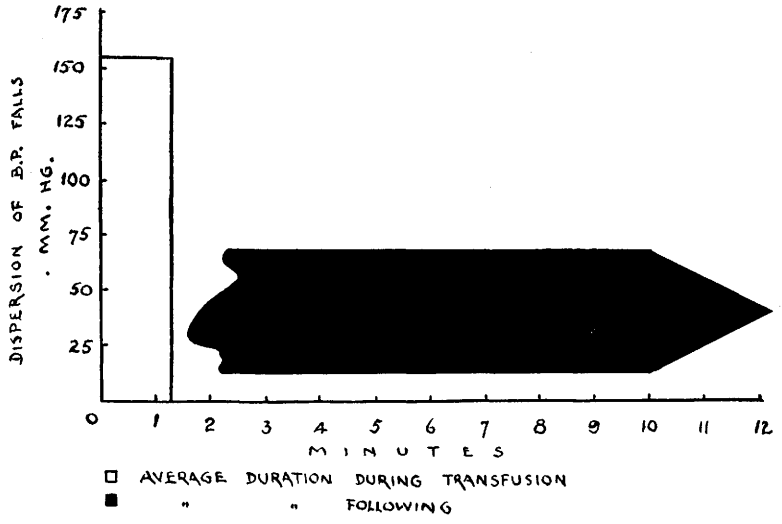

TABLE I.
Normal Donor and Hypertensive Recipient.

No.	Quantity blood (cc)	Initial B.P. (mm Hg)	Transfusion fall Depth	Transfusion fall Duration	Duration transfusion	Prolonged fall Depth	Prolonged fall Duration	%
					min sec			
2	180	197	0		4 0	68	9 min +	35
3	100	187	0		1 10	56	9 " +	30
4	160	182	0		2 0	29	15 " +	16
5	200	200	0		3 2	69	6 "	35
8	100	162	155	2 min 5 sec	4 0	11	12 " +	6
9	25*	179	0		1 0	46	31 " +	26
13	110	188	31	3 " 20 "	3 30	32	†7 " +	17

*A mixture of renal venous and femoral arterial blood.
†The pressure was still falling when a technical accident interfered.

These changes were easily differentiated from the predictable, prolonged depressions that persisted after cessation of the transfusions. Graph 1 demonstrates the scattering of the extent against the average duration of this "incompatibility" effect as compared to the prolonged blood pressure changes that occurred within experimental expectations.

Table I contains the results of transfusing hypertensive dogs with the blood of normal donors. Seven experiments were done.

Experiments were usually stopped when the recipients' pressures began to rise to the initial levels.

An attempt was made to stimulate the production of antipressor substance by the normal kidneys of donor dogs in all the above experiments except Nos. 8 and 9. In order to do so donors were given

TABLE II.
Normal Donor and Normal Recipient.

No.	Quantity blood (cc)	Initial B.P. (mm Hg)	Transfusion fall			Duration transfusion		Prolonged fall Depth
			Depth	Duration				
				min	sec	min	sec	
6	120	130	130	0	30	3	0	0
7	200	154	17	0	34	3	2	0
11	150	153	0			2	50	0
12	120	165	0			2	10	0

approximately 25 cc of crude renin made according to the method of Grossman.[2] In earlier experiments saline extracts of kidney were used with similar results. The blood for transfusion was drawn at an arbitrary point where the recorded pressure curve regained the baseline. It was thought that the antipressor effect would probably be most prominent at this time. This needs further investigation.

Four experiments were carried out using normal donors and recipients. The donor of No. 11 received renin, the others did not (Table II).

No. 6 exemplifies a precipitous fall to a shock level and recovery during transfusion. No prolonged falls occurred. The blood pressures of unoperated dogs were often elevated in comparison with their preanesthesia levels. On the contrary, dogs with clamped renal arteries showed moderate depressions of pressure under anesthesia. The explanation is obscure.

Table III shows the effects of transfusing hypertensive dogs with blood of hypertensive donors. The donors had pressures of over 200 mm of mercury with and without anesthesia.

Immediately upon stopping the transfusion the pressure in No. 14 regained its initial hypertensive level.

A tendency appeared for the pressure to fall in direct proportion to the initial height. However, the limited number of observations is insufficient to establish the tendency as a rule.

Discussion. Houssay and Fasciolo[3] raised the blood pressure in

TABLE III.
Hypertensive Donor and Hypertensive Recipient.

No.	Quantity blood (cc)	Initial B.P. (mm Hg)	Transfusion fall			Duration transfusion		Prolonged fall Depth
			Depth	Duration				
				min	sec	min	sec	
1	200	194	0			5	40	0
14	200	194	56	4	26	4	30	0

[2] Grossman, E. B., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 40.

[3] Houssay, B. A., and Fasciolo, J. C., *Rev. soc. argent. biol.*, 1937, **13**, 284.

nephrectomized dogs by implanting ischemic kidneys into their necks. Recently, Solandt, Nassim and Cowan[4] demonstrated a rise in pressure of normal, nephrectomized dogs by cross-transfusion with hypertensive ones. This suggests that a pressor substance is produced by the kidney and is mediated through the blood stream. The experiments described above attempt to demonstrate the presence of an antipressor substance in the blood of dogs with intact kidneys and its absence in those with clamped renal arteries and hypertension. The antipressor effect is demonstrable only in hypertensive animals. Since the beginning of this work, Harrison, Grollman and Williams[5] and Page, Helmer, Kohlsdaedt, Fouts, Kempf and Corcoran[6] reported a latent and prolonged reduction of hypertension with material chemically extracted from kidneys. Although the crude materials used by them contain impurities, their work plus the demonstration of the absence of an antipressor effect in blood of dogs with partially occluded renal arteries given here indicate that the kidneys produce an antipressor substance. These experiments show that the antipressor effect is mediated through the blood stream. There appears to be an equilibrium in the circulation of normal dogs between a substance that tends to elevate the blood pressure and one that acts to prevent its elevation.

Transfusions between dogs that cross-match satisfactorily may cause deep falls of short duration that are clearly distinct from the physiological response of hypertensive dogs to the addition of nonhypertensive blood.

Conclusions. Blood of dogs with intact renal circulations reduces the blood pressure of those made hypertensive by partially occluding the renal arteries. Blood from hypertensive dogs gives no such effect. Blood of normal dogs contains an antipressor substance that is absent in hypertensive dogs. Normal blood pressures are not affected by it.

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4 Solandt, D. Y., Nassin, Reginald, and Cowan, C. R., *Lancet*, 1940, **1**, 873.

5 Harrison, T. R., Grollman, Arthur, and Williams, J. R., Jr., *Am. J. Physiol.*, 1940, **128**, 716.

6 Page, I. H., Helmer, O. M., Kohlsdaeht, K. G., Fouts, P. J., Kempf, G. F., and Corcoran, A. C., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 722.