TABLE I.

	Pressor	Unchanged	Depressor
Benign hypertension	1	4	3
Malignant "	0	0	2
Nephritis			
Acute	1	0	3
Subacute or chronic	0	1	2
Polycystic kidney	0	0	1
Total	2	5	11

a depressor effect during the severe active phase when the blood pressure was elevated and a definite pressor effect when the level of the blood pressure declined toward normal level.

This evidence does not favor the existence of a direct peripherally acting circulating pressor substance in hypertension. If, as is likely in renal hypertension, a humoral substance exists which is responsible for the hypertension, it is not like epinephrin, pitressin or other substances having a direct pressor effect, or else not sufficiently pressor so as to be detected by this method.

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Nature of Peripheral Resistance in Arterial Hypertension.

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The arteriolar hypertonus responsible for hypertension is to be explained by one of the following mechanisms: 1. Increase in sympathetic vasoconstrictor impulses. 2. Circulating pressor substances. 3. A local disturbance in the vessels themselves.

The first factor has been ruled out since anesthetization of vasomotor nerves does not release the vascular hypertonicity.[1]

That there is no increase in circulating pressor substances in the blood of patients with hypertension is indicated by the following experiments. Direct cross transfusions were performed between patients with malignant hypertension and subjects with normal cardiovascular systems (these subjects had inoperable carcinomata). Two Unger sets were employed simultaneously so that at no time was there an appreciable change in blood volume in either patient.

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1 Prinzmetal, M., and Wilson, C., *J. Clin. Invest.*, 1936, **15**, 63.

Four such procedures were carried out, the amounts of blood interchanged being 500, 700, 1460 and 2000 cc. respectively. Congo red was injected into one subject before the transfusion. Forty-two percent of the dye was found in the blood of the other subject at the completion of the experiment.

If hypertension is due to a circulating pressor substance, a rise in blood pressure should be expected in the normal subjects with large amounts of hypertensive blood and a fall in pressure in the hypertensive patients with equivalent amounts of normal blood. No such changes were observed in either group.

Experimental hypertension was produced in dogs by the Goldblatt technique.[2] The tails of such dogs were then perfused alternately with their own heparinized or citrated arterial blood and with blood from normal dogs. A constant volume pump was used and the pressures required to force the blood through the tissues compared. In 4 instances the blood from the hypertensive dogs had a depressor effect and in one case a pressor effect as compared with blood from normal dogs.

Perfusion of denervated normal and hypertensive organs with Tyrode's solution was performed. Ischemia was produced by stopping the perfusion for varying periods of time. It was found that following this procedure the vessels first dilated and then gradually resumed their former tonicity (reactive hyperemia). These observations emphasize the importance of local factors for the maintenance of vascular tonus independent of nervous impulses or of circulating pressor substances.

It is well known that hypertension may occur following disturbances in renal function. Since the arteriolar hypertonus is not neurogenic in origin,[1] it must be mediated through a humoral mechanism. The evidence presented in this and the preceding[3] paper indicates that this circulating substance is not directly pressor in itself. It is concluded that in renal hypertension a circulating substance arising directly or indirectly from the kidney, and not directly pressor in itself elicits the pressor response locally in the vessels themselves by some unknown mechanism. Whether the mechanism of essential hypertension is of a similar nature is unknown. The evidence indicates, however, that since the vascular hypertonus is not neurogenic in origin[1] nor due to a circulating substance having a direct pressor effect on the vessels the difficulty must lie apparently in the vessels themselves, although this too may be mediated in some unknown manner through a humoral mechanism.

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[2] Goldblatt, H., *et al., J. Exp. Med.*, 1934, **59**, 347.

[3] Friedman, B., and Prinzmetal, M., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 543.