Accordingly, juice was collected by Greenspon's technique, and 80 cc. of juice, incubated at 37°C. for 2 hours, and 80 cc. boiled tomato juice, adjusted to pH 7.0, were administered orally in a single dose to a pernicious anemia patient with red cells at 2,100,000. The reticulocytes were 2.5% and never rose above that level during the next 10 days, the red cells fell to 1,600,000. There was a subsequent rise of reticulocytes to 31% on adequate parenteral liver extract. Another patient with red cells at 1,900,000 received 80 gm. of boiled liver, hashed to a paste, with 80 cc. of boiled tomato juice in a single dose. Reticulocytes rose from 3.3% to a peak of 8.4 on the eighth day, with no change in the red cell level. After the reticulocytes had fallen to 3.3%, 80 gm. of boiled liver paste and 80 cc. of normal juice, collected by Greenspon's technique, were incubated at 37°C. at pH 7.0 for 2 hours, and administered with boiled tomato juice. The reticulocytes rose to 14.6% on day 7 and fell to 8.5% 3 days later when 80 gm. of boiled liver paste and 80 cc. of normal juice collected without alkali, but adjusted to pH 10 for 30 minutes and then incubated with the liver for 2 hours at pH 5.5 were given in tomato juice. The reticulocytes rose to 19.8%, the red cells to 2,100,000 six days later.

Summary. Exposure of normal human gastric juice to pH 10 for 30 minutes destroys peptic activity without materially affecting intrinsic factor. Pepsinogen containing 28 mg. N was inert when administered parenterally. Eighty cc. of normal juice collected by Greenspon's technique was inert but when added to 80 gm. of boiled liver accentuated the hematopoietic effect of the liver.

8693 P

Vasomotor Effects of Blood in Patients with Hypertension.

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Many investigators have noted increased pressor (or diminished depressor) substances in the blood of patients with hypertension.[1-4]

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1 Major, R. H., *Arch. Int. Med.*, 1927, **40**, 891.

2 Lange, F., *Klin. Wchnschr.*, 1933, **12**, 173.

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4 Marx, H., and Hefke, K., *Klin. Wchnschr.*, 1933, **12**, 1318.

Others frequently employing similar methods, have failed to find them.[5-9] We have used the denervated rabbit's ear preparation as described by Pissemski[10] and modified by Katz[11] to compare the effect of blood of persons with hypertension and subjects with normal blood pressures. This preparation has been found to be sensitive to known pressor substances in high dilutions (epinephrine 1 to 100,000,000 and pitressin 1 to 150,000), and has an important advantage in that whole undiluted relatively unchanged blood plasma may be used. In the early experiments the inflow pipette was connected to a Mariotte bottle. Subsequently we found a constant volume pump to be more satisfactory.

The perfusion was started with Tyrode's solution and followed with unheated plasma alternating between blood from normal and hypersensitive individuals and noting the changes in pressure with constant inflow. Either citrate or heparin was used as anticoagulant. Generally about one hour elapsed between the time of withdrawal of the blood and the beginning of the experiment.

Eighteen patients with hypertension have been studied. These comprise 8 with benign hypertension, 2 with malignant hypertension, 7 in various stages of glomerulo-nephritis and one with polycystic kidney disease. The effect of the plasma as compared with that of the normal control is summarized in the table.

In 16 cases there was a depressor or no effect and in only 2 instances was there a definite pressor effect of the blood from the subject with hypertension over that from the individual with normal blood pressure. These changes could not be attributed to variations in viscosity or surface tension, since these properties varied only slightly and in no consistent direction. The addition to the test plasma of minute amounts of known pressor substances such as epinephrin and pitressin was followed by a well defined pressor response.

Three patients with acute glomerular nephritis were studied during different phases of their disease. In one instance a depressor effect was observed during the active phase with hypertension and also following recovery. In the other 2 subjects there was evident

5 Aitken, R. S., and Wilson, C., *Quart. J. Med.*, 1935, **4**, 179.

6 Turriès, J., and Robert, S., *Presse méd.*, 1930, **38**, 85.

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8 Capps, R. B., Ferris, E. B., Taylor, F. H., and Weiss, S., *Arch. Int. Med.*, 1935, **56**, 864.

9 De Wesselow, O., and Griffiths, W. J., *Brit. J. Exp. Path.*, 1934, **55**, 45.

10 Pissemski, A., *Pflüger's Arch.*, 1914, **156**, 430.

11 Katz, G., *Arch. internat. de pharmacodyn. et de thérap.*, 1934, **49**, 239.

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.

8694 P

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.

* Sutro Fellows for Cardiovascular Research.

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