teriological diagnosis of pneumonia. A consecutive series of 105 specimens received for examination in the Health Department, Pneumonia Control Division Laboratories, were cultured, using one plate containing sulfapyridine 10 mg % and one control without sulfapyridine, to determine whether sulfapyridine-resistance occurs regularly and frequently in such specimens. Eighty-three of the 105 specimens contained pneumococci. The susceptibility of 35 of these pneumococcus strains was determined within 24 hours by direct inoculation of the specimens on blood agar plates, and of 29 by the use of subcultures which required 48 hours or longer. Subcultures were not obtained from 19 specimens. The direct inoculation of specimens on blood agar plates was successful most regularly (24 of 37 specimens) when the specimen showed a type-specific pneumococcus by Neufeld examination.

All of the microörganisms obtained from the 64 fully tested specimens (56 patients) were susceptible to the bacteriostatic action of blood agar plates containing 10 mg % of sulfapyridine.

The property of resisting the bacteriostatic action of sulfapyridine comparable in degree to that produced experimentally may appear as a characteristic of pneumococci in human pneumococcus infections where therapeutic response does not occur. Such resistance may be recognized by the observation of the growth on blood agar plates containing sulfapyridine. The diagnostic procedure outlined is recommended for use in pneumococcus infections that do not respond satisfactorily to chemotherapy with sulfapyridine.

11953 P

Changes of Arterial Blood Pressure and Renal Hemodynamics by Injection of Angiotonin in Human Beings.

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Renin, the so-called "renal pressor substance" is vaso-inactive unless permitted to interact with a pseudoglobulin present in blood plasma, which has tentatively been denominated "renin-activator."[1] The interaction of renin and renin-activator yields a crystallizable,

[1] Kohlstaedt, K. G., Helmer, O. M., and Page, I. H., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 214.

dialyzable, thermostable product, angiotonin.[2] Intravenous injections of this substance in normal animals cause sharp pressor responses which diminish slowly with repeated injections. Nephrectomized animals are highly sensitive to the pressor action of this substance and do not show tachyphylaxis with repeated injections.[3] Slow intravenous infusions of angiotonin in dogs increase arterial pressure and cause renal vasoconstriction, predominantly of the glomerular efferent arterioles, but do not alter cutaneous temperatures.[4] The effects of angiotonin infusion therefore simulate those of renin,[5] although they are not as long sustained.

The present report is concerned with observations of blood pressure and renal hemodynamics during single injections and intravenous infusions of angiotonin into human beings. Electrocardiographic records and observations of venous pressure and skin temperature were obtained in some instances. These, together with further observations of renal functional changes will form part of a subsequent report.

Arterial pressure was determined by auscultation. Effective renal blood flow was calculated from the hematocrit ratio and apparent plasma diodrast clearance and is equal to approximately 90% of total renal blood flow.[6] Diodrast was determined in blood and urine by a modification of the method of White and Rolf[7] and inulin by the method of Corcoran and Page.[8] A mixture of diodrast, phenol red and inulin in 0.9% NaCl was given intravenously at a slow rate during the observations of renal clearances.[9]

The angiotonin solutions were prepared by the method of Helmer and Page.[2] The responses to single injections of angiotonin were observed only with reference to arterial pressure, while diodrast and inulin clearances were observed during the infusions of angiotonin. The infusions were preceded by a single dose, intravenously, of 1.0 to 1.5 cc of the angiotonin solution and continued by small injections of the solution into the rubber tubing which carried the diodrast-inulin infusion.

Single Injections. Single intravenous injections of from 0.5 to

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2 Page, I. H., and Helmer, O. M., *J. Exp. Med.*, 1940, **71**, 29.

3 Page, I. H., and Helmer, O. M., *J. Exp. Med.*, 1940, **71**, 495.

4 Corcoran, A. C., and Page, I. H., *Am. J. Physiol.* 1940, **130**, 335.

5 Corcoran, A. C., and Page, I. H., *Am. J. Physiol.*, 1939, **126**, 354.

6 Corcoran, A. C., Smith, H. W., and Page, I. H., *Am. J. Physiol.*, 1940, **129**, 338.

7 White, H. L., and Rolf, D., PROC. SOC. EXP. BIOL. AND MED., 1940, **41**, 1.

8 Corcoran, A. C., and Page, I. H., *J. Biol. Chem.*, 1939, **127**, 601.

9 Smith, H. W., Goldring, W., and Chasis, H., *J. Clin. Invest.*, 1938, **17**, 263.

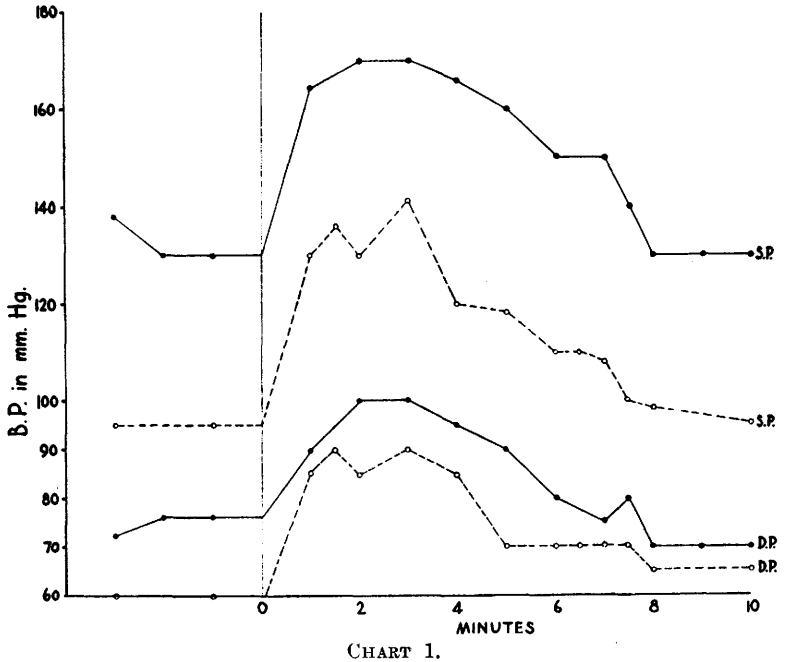

CHART 1.

Effects of single intravenous injections of angiotonin on arterial blood pressures in two patients. Patient 1. •——• Dose injected 0.6 cc. Patient 2. o- - o Dose injected 1.0 cc. Ordinate: Systolic (S.P.) and diastolic (D.P.). Blood pressure in mm Hg. Abscissa: time in minutes.

1.0 cc of angiotonin increase both systolic and diastolic arterial pressure. The arterial pressure returns to its normal value at the end of 6 to 9 minutes. The injections are not associated with subjective discomfort, nor do they cause pallor nor other outward vasomotor change. A graphic chart of 2 such injections (Chart 1) illustrates the typical response of normotensive patients.

Angiotonin Infusion. The graphic record of an experiment in which an initial intravenous dose of angiotonin was succeeded by a succession of smaller doses into the infusion fluid is shown in Chart 2. It will be noted that the increased arterial pressure is associated with decreased renal blood flow and with an increase of filtration fraction (ratio inulin/diodrast clearance) and that the pressor and renal responses subsided during the 19 minutes which followed the last addition of angiotonin to the infusing fluid.

Comment. The effects of intravenous injections and infusions of angiotonin in human beings closely resemble the effects of this substance in experimental animals. The increase of filtration fraction which occurs during angiotonin infusion is evidence of increased intraglomerular pressure[10] and, since it is associated with decreased

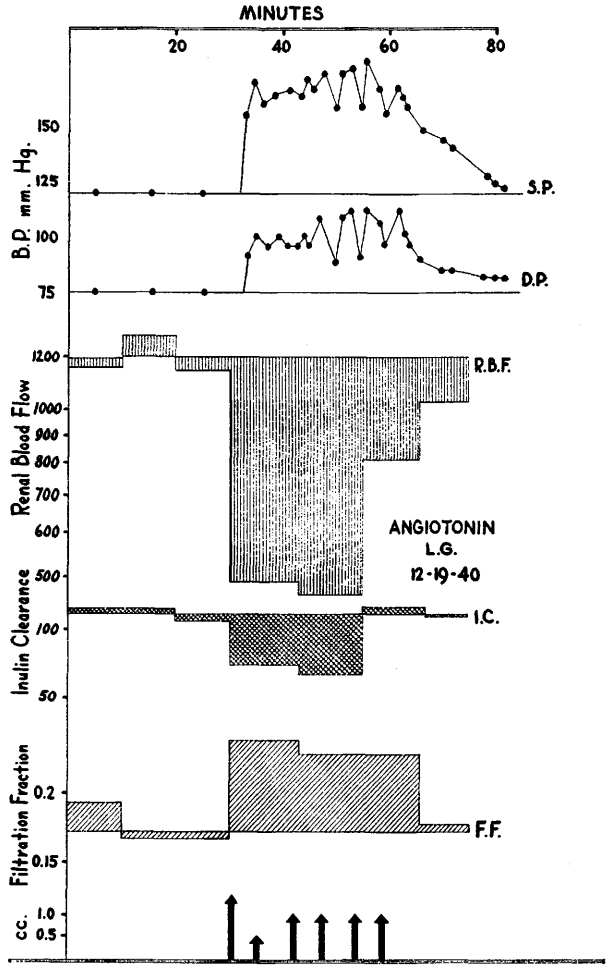

CHART 2.

Effects of infusion of angiotonin on arterial blood pressure, renal blood flow, inulin clearance and filtration fraction in patient L.G. Ordinates from above downwards: arterial systolic (S.P.) and diastolic (D.P.) blood pressures; effective renal blood flow (R.B.F.) in cc per min.; inulin clearance (I.C.) in cc per min.; filtration fraction (inulin/diodrast clearance ratio, F.F.); cc indicates volumes of initial intravenous injection of angiotonin and of subsequent injections into the infusing fluid. Effective renal blood flow, inulin clearance and filtration fraction are plotted semilogarithmically. Abscissa: time in minutes.

renal blood flow, is the characteristic result of constriction of the glomerular efferent arterioles. Efferent arteriolar constriction with absolutely or relatively decreased renal blood flow characterizes the kidney in hypertension in human beings.[11] Since the blood of

[10] Chasis, H., Ranges, H. A., Goldring, W., and Smith, H. W., *J. Clin. Invest.*, 1938, **17**, 683.

[11] Smith, H. W., The Porter Lectures, Univ. of Kansas, 1939.

patients suffering from hypertension contains an excess of a vasoconstrictor which, like angiotonin, is potentiated in the presence of the blood of nephrectomized animals,[12] it is not unlikely that the increased arterial pressure and altered renal hemodynamics of hypertension may be the result of the unopposed action of angiotonin.

11954 P

Relationship of Vitamin A Blood Level in the Rat to Vitamin A Intake and to Liver Storage.

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This study was undertaken to determine whether the concentration of vitamin A in the blood has any relationship to the vitamin A intake and to the storage in the liver. Groups of albino rats, 3 to 4 weeks of age, were fed amounts of vitamin A ranging from 0 to 1000 international units daily. The vitamin A supplement used for rats receiving 100 units or less daily was a reference cod liver oil obtained from the United States Pharmacopea Committee, whereas rats receiving 1000 units were given a vitamin A concentrate. After the rats received these preparations for 6 weeks, the vitamin A content of their bloods and livers was determined 24 hours after the last dose of the vitamin.

The method employed for the vitamin A determination of the blood and liver was based on the Price-Carr reaction. As the diet was devoid of carotene, this substance was not found in the blood or livers of the rats. The vitamin A in the blood was extracted directly with petroleum ether and alcohol as recommended by Clausen and McCoord,[1] whereas the liver was treated by a preliminary saponification. The extracts were evaporated in nitrogen, taken up with chloroform and then treated with antimony trichloride. The intensity of the resulting blue color was measured at 620 mμ with the use of an Evelyn Photoelectric Colorimeter.[2] The reading was translated into biological units (international) by re-

[12] Page, I. H., *J. Exp. Med.*, 1940, **72**, 301.

[1] Clausen, S. W., and McCoord, A. B., *J. Pediatrics*, 1938, **13**, 635.

[2] Dann, W. J., and Evelyn, K. A., *Biochem. J.*, 1939, **32**, 1008; Kimble, M. S., *J. Lab. Clin. Med.*, 1939, **24**, 1055.