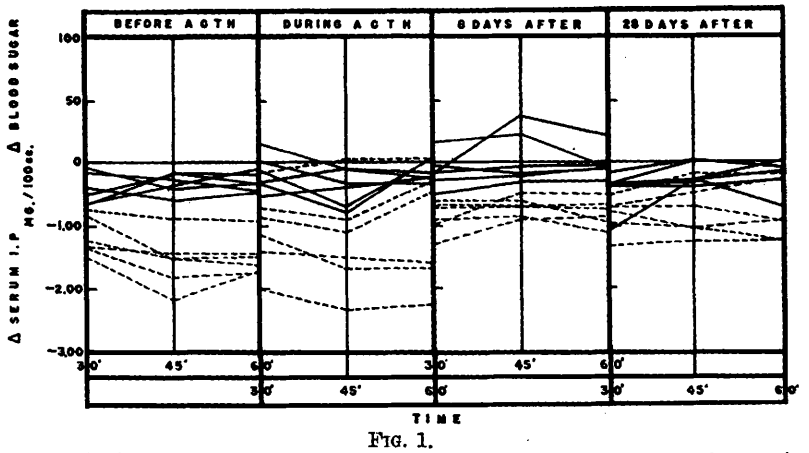

FIG. 1.

The individual variations of blood sugar (solid lines) and serum inorganic phosphorus (dotted lines) from the initial values during the different periods of the experiment.

tion of glucose alone(18) that occurs under the influence of ACTH is not due to a deficiency in insulin production. It was possible to observe that the changes of blood sugar tended to appear and disappear sooner than the modifications in inorganic phosphorus which suggest that they are independent in its mechanism although closely related phenomena. It may be that these experiments could be interpreted as an *in vivo* reduction of the rate of phosphorylization induced by adreno-cortical stimulation.

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Effect of Renal Venous Occlusion on Intrarenal Pressure.* (18629)

H. G. SWANN, A. V. MONTGOMERY, AND JAMES S. LOWRY.

From the Carter Physiology Laboratory, University of Texas Medical Branch, Galveston.

When the veins leaving a tissue are occluded, the hydrostatic pressure from the heart is in part transmitted into the tissue. Burch and Sodeman(1) and Wells, *et al.*(2) found an increase in subcutaneous tissue pressure of 1-3 cm H_2O during prolonged venous congestion. In muscles the same occurs: Wells, *et al.*(2) report that in venous congestion, the intramuscular pressure of the gastrocnemius rises 20 cm H_2O and that of the soleus rises 50 cm H_2O. In the case of the kidney, we have reported that renal venous occlusion causes a pronounced rise in the pressure within the kidney parenchyma(3,4). Gottschalk(5) has also studied the same phenomenon, reporting that the intrarenal pressure does not rise with partial renal venous occlusion until the renal venous pressure exceeds the preexisting interstitial pressure. The present study will describe further experiments in which the effect of both partial and total renal venous occlusion on intrarenal

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pressure was measured.

Methods. Dogs under sodium pentobarbital anesthesia were used. After exposing the kidney, the intrarenal pressure was measured by the transduced equilibrium method of Swann, Montgomery, Davis and Mickle(6); this entails injecting a small volume of fluid into the kidney by means of a nearly isometric manometer. When the manometer ceases moving, it has stopped forcing fluid into the tissue; its pressure at this point, which is optically recorded, is a measure of the intrarenal pressure; the latter will be designated, for purposes of brevity, as the IRP. Arterial blood pressure was measured, after cannulation of the carotid artery, by optical methods employing a glass Bourdon tube manometer (7). The renal vein was partially or totally occluded by a tourniquet, the degree of occlusion being controlled by the number of turns made on the tourniquet. The pressure in the renal vein on the kidney side of the occlusion was measured thus: a stiff plastic ("Saran") tube, with a 2 mm bore, filled with heparinized saline, was inserted into the right external jugular vein and then manipulated down the vena cava and into the left renal vein. Its tip was set on the kidney side of the occluding tourniquet. The pressures in this tube were also recorded by a Bourdon tube manometer. They will be designated by the abbreviation VP_R.

Results. Total occlusion. When the renal vein was totally occluded, the IRP was instantaneously elevated, as shown in Table I, from a mean of 25 mm Hg up to 76 mm Hg. In 5 out of the 11 dogs (Nos. 2, 8, 9, 10 and 11), the IRP rose to approximately the simultaneous diastolic pressure, but in the remaining 6, the IRP increased to a level definitely less than the diastolic pressure. In total venous occlusion the rise in IRP cannot in fact be closely related to any component of the simultaneous arterial blood pressure: neither to the systolic nor to the diastolic nor to the pulse nor the average nor to the product of pulse rate times pulse pressure, as inspection of the table will reveal. But it does rise to the same pressure, as shown by the encircled points in Fig. 1, as the simultaneous VP_R.

TABLE I. Effect of Total Renal Venous Occlusion on Intrarenal Pressure.

Dog No.	Intrarenal pressure		Blood pressure		Heart rate
	Before occlusion	During occlusion	Systolic	Diastolic	
1	36	57	153	98	238
2	14	55	137	57	164
3	15	63	130	75	89
4	35	77		105	131
5	18	48		138	167
6	10	83		105	160
7	23	95	162	105	166
8	59	124	172	120	138
9	27	90	142	98	214
10	15	40	75	40	253
11	18	109		100	105
Mean	25	76			

Partial occlusion. The data for 5 dogs are shown in Fig. 1. When the renal vein is partially occluded, the IRP is not affected until the VP_R is elevated above the initial IRP. As the occlusion is further increased, thus increasing VP_R, IRP rises with the VP_R in a one-to-one relationship. When the occlusion is complete, the IRP is the same as the simultaneous VP_R as indicated in the figure.

The VP_R in total occlusion does not consistently rise, just as the IRP does not rise, to the simultaneous diastolic blood pressure. Records were obtained on this point in 4 dogs: in the first, when the VP_R with total occlusion was 78 mm Hg, the simultaneous diastolic pressure was 100, in the second the 2 pressures were 84 and 82, in the third 85 and 110 and in the fourth 98 and 115.

Discussion. When the venous outflow of an organ is completely blocked, the simultaneous venous pressure rises to arterial pressure (8,9). But in the present experiment, the venous outflow was not completely blocked since the capsular circulation remained intact. This collateral circulation, irregular though it

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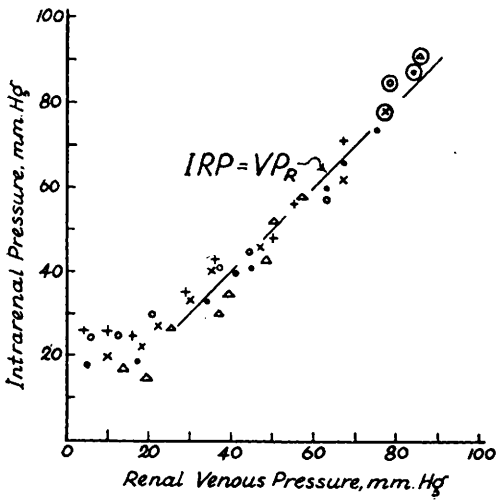

FIG. 1.

Relation of intrarenal pressure and renal venous pressure during venous occlusion. Individual records of 5 dogs. Encircled values are taken after complete occlusion.

is, undoubtedly drained away some blood when the main renal vein was occluded, and thus the renal vein pressure did not always rise to the simultaneous arterial pressure. When the VP_R is increased by partial occlusion to or above the control IRP, it causes the IRP to rise to the simultaneous VP_R. Gottschalk(5) has reported this likewise. The same general phenomenon was studied in arm veins by Ryder, *et al.*(10), who showed that the pressure in arm veins (when adjusted to heart level) is equal to the tissue pressure, and that when the arm veins are partially occluded with a cuff, the distal venous pressure at once rises just above the cuff pressure.

The close correspondence of IRP and VP_R (above the control IRP) furnishes confirmation of our hypothesis that the IRP measures the pressure within the renal venules(11). Furthermore, the fact that the IRP is not influenced until the VP_R rises above 25 mm Hg confirms our hypothesis that the pressure in these same vessels is also at about 25 mm. Moreover, because the IRP has been found to be so uniform through all the renal parenchyma(6), it is also presumed that this pressure is transmitted to all the tubes in the kidney. Hence, in order for fluids to flow through the various tubes, their pressures must be greater than the IRP or else they would collapse. Arteriolar and glomerular pressures are undoubtedly higher than the IRP, but all other renal tubes are thought to have a pressure of about 25 mm Hg: the peritubular capillaries and venules, the lymphatics and the entire uriniferous tubular system with its intracapsular space(11).

The characteristics of fluid flows through a system like that postulated are of considerable interest. In order to gain some insight into them, the behavior of the model illustrated in Fig. 2 was studied. Reservoir H delivered water into elastic tube E (actually "Penrose" tubing, I.D. 12.8 mm) and thence to outlet V, at which flow rates were measured. The elastic tube E was surrounded by the rigid, water-filled cylinder K, the pressure in which was controlled by reservoir T. The pressures in reservoir H and reservoir T will be designated by the symbols H and T respectively. (Air bubble C prevented the system from "bouncing".) The lateral pressures at A and B were also measured. At O, an adjustable, occluding tourniquet was placed so that the flow, and hence the pressure, at B could be readily varied after flows of water through the system had been established. When pressure T was imposed upon elastic tube E, little or no flow took place until pressure H exceeded pressure T. Regardless of the pressure at H, if it exceeded T, the pressure at A was just slightly greater than pressure

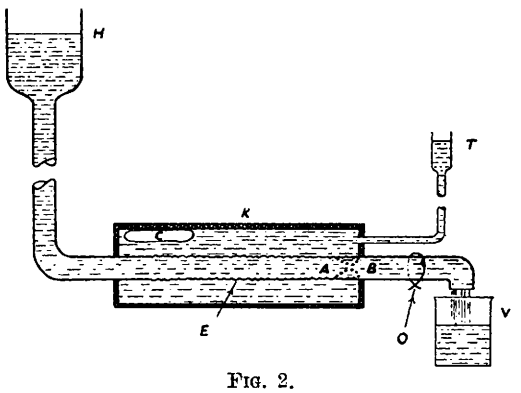

FIG. 2.

Model used for studying pressure and flow relations. See text for explanation.

10. Ryder, H. W., Molle, W. E., and Ferris, E. B., *J. Clin. Invest.*, 1944, v23, 333.

11. Montgomery, A. V., Davis, J. C., Prine, J. M., and Swann, H. G., *J. Exp. Med.*, 1950, v92, 637.

T, while the pressure at B, only a millimeter or two downstream, dropped almost to zero.

In this model, cylinder K is equivalent to the kidney and pressure T is equivalent to the renal tissue pressure, while reservoir H represents the hydrostatic pressure of the blood given by the heart. Furthermore, pressure T is imposed on the whole length of E until tube E emerges from cylinder K; at this point the pressure suddenly drops almost to zero.† Continuing the analogy, IRP is imposed on peritubular capillaries, venules, lymphatics and tubules until they emerge from the kidney. At this point, the pressure in them suddenly drops toward zero—actually, in the case of the veins, toward vena cava pressure. Now, renal vein pressure has been reported to be 11 mm Hg(12), or only a few millimeters above caval pressure. This is similar to taking a pressure at B. If in such experiments the catheters used to measure renal venous pressure were inserted all the way to A, then, it is postulated, the renal venous pressure would be found just to exceed IRP. The point of pressure change is undoubtedly somewhere above the epithelial lining of the pelvis. Here the pressure abruptly rises, it is thought, to 25 mm Hg.

When tourniquet O is tightened so that the pressure at B is elevated, no change in the rate of flow occurs until pressure B exceeds pressure T. Thus, if T is 25 mm Hg, pressures at B, induced by tightening tourniquet O, of 10 or 15 or 20 mm Hg do not slow the flow of water out of the system. It is only when the pressure at B is 25 mm or greater that flow is slowed. The same situation pertains in the kidney, for both Blake, *et al.*(13) and Selkurt, *et al.*(14) have demonstrated that renal blood flow is not appreciably influenced by renal vein pressures up to some 22 mm Hg. In the experiments of Blake, *et al.*(13), it was only when the renal vein pressure was raised to 40 mm Hg that renal blood flow was slowed. This fact furnishes good confirmation from independent sources of observation that the IRP is above 22 mm Hg. Similarly, if there were a pressure of 25 mm Hg in the renal tubules, one would not expect that urinary flow rate to change unless ureteral pressure exceeded 25 mm. This in fact has been demonstrated by Pilcher, *et al.* (15): in normal dogs, ureteral pressures of 22 mm Hg do not slow urine flow but 29 mm of pressure does. The relatively low value of 10 mm Hg, reported by Winton(16) in the same experiment, is thought due to the fact that he was studying such a relatively abnormal preparation, *viz.* the isolated perfused kidney(17,18).

It has been pointed out that the intrarenal pressure is exceptionally high for a tissue pressure(11). Furthermore, it has been shown that the venous pressure of subacute congestive heart failure, elevated though it is, does not exceed the exceptionally high IRP(19). It was therefore suggested(19) that the IRP is normally, as it were, "set high" so that random or pathological fluctuations in vena cava pressure do not influence renal blood flow or renal tubular function. Something akin to this has been done in the present experiment, in which elevations in the renal venous pressure exert no influence on IRP until they exceed it. Because vena cava pressure is so much smaller than IRP, it does not, as in the studies on the model reported here, and as in the experiments of Blake, *et al.*(13) and Selkurt, *et al.*(14), influence renal blood flow until it exceeds the exceptionally high renal tissue pressure. This situation permits the whole delicate interplay of tubular processes to continue at a relatively constant pressure.

† In the model, there can be perceived a constriction between A and B (indicated by dotted lines), the magnitude of which is directly proportional to the ratio of pressure A to pressure B.

12. Maxwell, M. H., Breed, E. S., and Schwartz, I. L., *J. Clin. Invest.*, 1950, v29, 342.

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This theory presumes that hydrostatic pressure, either blood or tubular or interstitial, is held constant in the tubular sections of the nephron; these constant pressures are presumed to play no role in the process of absorption. Rather, the differential absorptive process is governed entirely by fluctuating oncotic pressures and cellular metabolic processes.

Summary. 1. When the renal vein is completely occluded, the intrarenal pressure increases about 3-fold, being elevated to the simultaneous pressure in the vein on the renal side of the occlusion. Usually this pressure is somewhat less than the simultaneous diastolic blood pressure. When the vein is partially occluded, intrarenal pressure does not change until the simultaneous pressure in the vein on the renal side of the occlusion rises to the original intrarenal pressure. At this point, as the occlusion is increased, the two pressures rise together and always have the same value. 2. The hypothesis is proposed that the pressure inside the renal peritubular capillaries, venules, uriniferous tubules and lymphatics is normally just above intrarenal pressure, *i.e.* at 25 mm Hg. This situation, it is postulated, permits the process of reabsorption to take place freed from the influence of random or pathological fluctuations in vena cava pressure. Oncotic pressures and cellular metabolic processes, therefore, are presumed to be the primary determinants of differential reabsorption.

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Resistance Lowering Effect of Human Respiratory Tract Mucin.* (18630)

W. J. NUNGESTER, J. K. BOSCH, AND DARWIN ALONSO.
From the Department of Bacteriology, University of Michigan.

Although hog gastric mucin has been extensively used since 1932(1) to lower the resistance of laboratory animals to bacteria, the possible role of excessive mucus accumulations on the defense mechanisms of man has received little attention. Because of the commercial availability of hog gastric mucin, this material has been used almost exclusively as an aid in producing experimental infections. The senior author in unpublished work has used human respiratory tract mucin in a few trials with results quite similar to those obtained with gastric mucin. It seemed desirable to confirm and extend these earlier unpublished observations with human respiratory tract mucin since there are many clinical situations where excessive mucus could be significant in lowering the resistance of man.

The human mucin used in this study was obtained from sputum collected from patients with varying lung conditions (lung neoplasms, bronchiectasis, lung abscess, asthma, suppurative pneumonitis). The different samples of sputum were homogenized together in a CO_2 atmosphere by means of a Waring blendor. The mucin was then sterilized by heating at 80°C for ten minutes. Sterility of the mucin was controlled by culture on a blood agar plate.

Intra-bronchial inoculations in rats. A small vertical incision was made through the skin and muscles overlying the trachea to aid in passing a number 5 French ureter catheter into a main bronchus. Although the exposed trachea was not opened, a clear view was had of the descending catheter. In this manner, passage of the inoculum into the esophagus was avoided with certainty. After inoculation, the skin incision was closed with a single suture. Four series of experiments were done, each consisting of 5 groups of 5 rats each. A suspension of pneumococci, type I, was suspended in different menstrums and 0.2 cc was injected intra-bronchially into each animal. Each rat received an inoculum of 10^{-4}

* Aided by a grant from the U. S. Public Health Service.

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