pregnant mice shows an increase in total purine, whereas the spleen does not.

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Pharmacology of Smooth Muscle Valve in Renal Portal Circulation of Birds.* (20841)

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The avian renal portal system, first described by Jacobson in 1822(1) was not proved functional until 1948 by Sperber(2). In the bird the external iliac vein (EIV) communicates with the internal iliac vein which drains into the renal parenchyma. The EIV also connects directly to the renal vein (RV) by a large venous shunt. Interposed at the point of communication from EIV to RV is a valve-like structure described by Spanner (3) which is of variable shape in various species of birds but which is composed of smooth muscle, and usually has a conical shape with single or multiple apical openings. When contracted, the valve would tend to divert iliac vein blood through the kidney and when relaxed, blood would pass directly into the renal vein. Sperber described the position and appearance of the valve (Fig. 1) and presumed that it regulated blood flow to the renal tubules. Sperber clearly illustrated the functional significance of the renal portal system in the chicken by demonstrating that phenol red injected into one leg appeared in excess in the urine of the ipsilateral kidney.

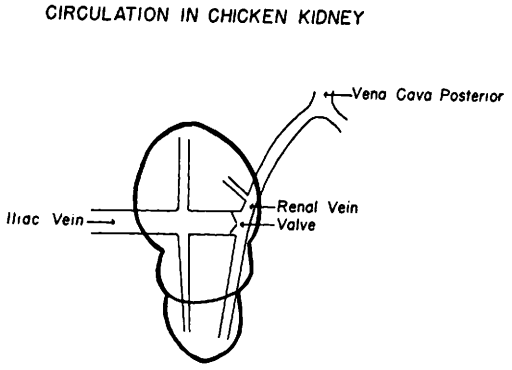

FIG. 1. Renal-portal circulation in chicken kidney.

The present report deals with the response of this valve to autonomic drugs as determined by direct recording of the response of the isolated structure suspended in a smooth muscle bath, and as estimated by the excess excretion of para-aminohippurate by one kidney when this substance was injected into the ipsilateral leg or iliac vein.

Method. In vitro. Valves were dissected from veins of freshly killed turkeys† weighing about 25 lb. The valve was suspended in oxygenated Tyrode's solution at 37.5°C in an Anderson muscle bath and attached to a light weight lever recording on a smoked drum. The bath volume was 30 ml. *PAH uptake* by chicken kidney slices was determined by the method of Cross and Taggart(4) with one modification. The final PAH concentration was 0.0013 M. Slice to medium ratios were calculated on a wet weight basis. *In vivo.* Hens were anesthetized with sodium barbital, 200 mg/kg intravenously and infused with 1 ml per minute of glucose-saline solution. Urine was collected separately thru plastic cups‡ sewed over the cloacal orifice of each ureter and the recovery of PAH in the urine

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‡ Designed and made by Mr. E. J. Toner.

FIG. 2. Response of excised turkey vein valve to autonomic drugs.

		mg
Ach	= Acetylcholine	.05
Atr	= Atropine	.50
Off	= 10 min. wait after wash	
H	= Histamine	.025
E	= Epinephrine	.010
Time	= 10 sec.	

was assessed when administered to the renal portal system unilaterally. The amount of PAH in the urine on the injected side when compared with the amount recovered from the control side gives an index of the magnitude of the functional renal portal circulation at the time of injection and hence reflects the tonic state of the valve. When the valve is tightly closed the recovery of unilaterally injected PAH would be much greater from the urine of the injected side than from the control kidney in the same animal. With the valve widely open one would expect to find nearly equal amounts of PAH excreted by the two kidneys.

Results. In vitro. Fig. 2 shows that the excised smooth muscle valve of the turkey renal venous system responded by contraction to acetylcholine. The increased tonus was immediately reduced by atropine, and further contraction by acetylcholine was prevented by the presence of atropine. Histamine contracted the valve and this contraction was relaxed by epinephrine and also by norepinephrine. In other experiments the response of the smooth muscle to acetylcholine was potentiated by physostigmine.

In vivo. In intact hens under urethane anesthesia, PAH injected into one leg was recovered in approximately equal amounts in the urine of the two kidneys, indicating that under these circumstances little or no iliac vein blood was diverted into the renal portal system. Under barbital anesthesia on the other hand, PAH similarly administered was recovered in great excess from the ipsilateral kidney, ranging from 2 to 15 times the excretion of the control kidney, and indicating that the portal shunt must have been closed by contraction of the valve.

Assuming, on the basis of the *in vitro* experiments, that the valve contracts under cholinergic influence, several experiments were carried out to assess the effect of atropine upon the portal system. Fig. 3 illustrates such an experiment. PAH was infused at a constant rate into one of the leg veins, and the PAH excretion by the ipsilateral kidney ranged from 7 to 10 times the excretion rate of the opposite kidney. Atropine injected intravenously in a dose of 1 mg/kg promptly reduced the relative excess of PAH excreted on the injected side.

In some hens the infusion of PAH into the vein of one leg resulted in no great excess of PAH excretion in the urine from the kidney on the infused side. The administration of atropine did not alter the ratio in these animals. It is probable that in these birds the valve was originally open and atropine was not able to relax it further.

To demonstrate that the action of atropine

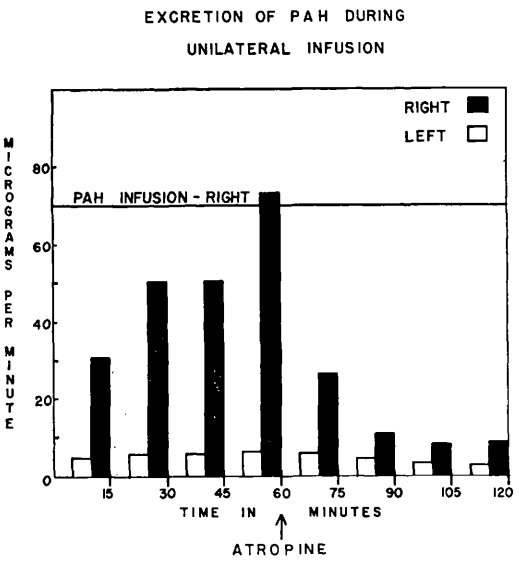

FIG. 3. Excretion of PAH from right and left kidneys when 70 μg/min. of PAH infused into right leg vein. After injection of atropine the previous abundant excretion from injected side was reduced possibly as a result of opening the venous valve.

TABLE I. Mean Values of S/M Ratios with Standard Error for PAH Uptake in Chicken Kidney Slices.

Exp.	Control	Atropine	Acetate	Atropine plus acetate
A	14.57 ± .639	12.88 ± .605*	19.45 ± .911	20.05 ± .684
B	15.32 ± .504	11.87 ± 1.054†	15.36 ± .587	16.46 ± 1.09

* 1:200000. † 1:100000. Acetate = 150 mg % final concentration.

must be due to relaxation of the venous sphincter rather than any direct inhibition of the tubular secretory mechanism, PAH uptake by chicken kidney slices was determined with and without added atropine. As shown in Table I, the PAH uptake by slices of chicken kidney in the presence of atropine was not significantly different from control slices. Table I shows the comparison of slice/medium wet weight ratios of chicken kidney tissue PAH uptake in controls with and without added acetate. Five observations were made for each value recorded. These results would indicate that the atropine-induced changes in the PAH excretion of the intact animal were not due to an effect on cellular PAH transport, but were more likely due to inhibition of the tone of the renal portal valve, permitting shunting of iliac venous blood directly into the renal vein.

Discussion. The experiments herein described suggest that the renal portal system of the chicken is not obligatory, as is the hepatic portal circulation, but is under the control of the autonomic nervous system.

Judging from the *in vitro* response of the renal portal venous valve to acetylcholine, atropine, and epinephrine, and from the *in vivo* response of the valve to atropine it could be concluded that this smooth muscle structure is contracted by a cholinergic mechanism and relaxed by adrenergic discharge. If one assumes that the response to emergency situations leads to sympathetic discharge in birds as in mammals, it follows that under conditions when muscular activity of the lower extremity is high, the renal portal shunt would remain open, permitting unimpeded venous return from the leg and reducing the volume load on the kidney. Under conditions in which leg blood flow would be expected to be minimal the valve would be closed and much of the iliac vein blood would traverse the renal parenchyma, increasing thereby the capacity of the tubular secretory and reabsorptive mechanisms.

It is of interest that this represents the only intraluminal vein valve which is known to contain smooth muscle. Perhaps the hepatic sphincter or Sperre valve, as it is known in the dog, is similar in function as are the smooth muscle bands in the hepatic veins of the seal and raccoon(5,6). The hepatic sphincter is contracted by histamine and relaxed by epinephrine. However, these structures are described as smooth muscle thickenings of the venous wall whereas the avian valve is a distinct conical smooth muscle structure affixed to the inner surface of the vein wall.

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