Venous Arterial Interactions Involving Serotonin in the Pampiniform Plexus of the Rat (37304)

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(Introduced by W. J. Bair)

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Single doses of epinephrine, norepinephrine and prostaglandins E_1, E_2 and $F_{2\alpha}$ injected into the spermatic vein of the rat have been observed to depress lateral pressure in the spermatic artery (1, 2). However, in these studies pressure never fell below 75% of pretreatment levels at any dose too small to affect central arterial pressure. In preliminary studies (3) involving spermatic vein injections of 1.0 μg/kg 5-hydroxytryptamine (serotonin), a more pronounced local affect on the spermatic artery pressure occurred such that blood flow through the testis was temporarily shut down. Long-term treatment of rats with subcutaneous serotonin is known to cause mild to severe damage to the seminiferous tubules (4, 5). Tracer studies with labeled serotonin (6) and angiographic studies (7) suggest that the extratesticular portion of the spermatic artery is the major site of serotonin binding and vasoactivity in the male reproductive tract. Additionally, for successful perfusion of the isolated testes of ram and goat (8) and the *in situ* testis of rat (unpublished data by the authors), it was necessary to include an antiserotonin in the perfusate. The following study was carried out in order to examine more closely the response of the spermatic artery to serotonin and, in particular, the venous–arterial interaction involving serotonin in the pampiniform plexus of the rat.

Materials and Methods. A total of 25 Sprague–Dawley male breeder rats (350–550*g*) were used in these studies. Anesthesia was maintained by oxygen–halothane inhalation through a tracheal cannula. Catheterization of the testis artery and vein and monitoring of flow and pressure were carried out as previously described (1, 9). Except where indicated, a miniature friction flowmeter (9) was installed in the descending intraalbugineal portion of the testis artery; and an infusion catheter was inserted into a small branch vein at the cranial pole of the testis. When venous pressure monitoring was required, a second small branch vein was catheterized. In 8 rats, testis artery flow distal to the pampiniform plexus was diverted to the femoral vein or to the distal part of the contralateral testis artery (Fig. 1). The first preparation (Fig. 1a) was designed to completely divorce the testis artery from a testis capillary bed while the second (Fig. 1b) maintained a link between artery and a testis while retaining the independence of artery and vein. In 4 rats with testicular catheters in place, the spermatic cords were attached to a linear displacement transducer so that smooth muscle activity in response to serotonin could be correlated with arterial pressure changes. Doses of serotonin (0.02–20 μg/kg) in 3 μl of warm (33.5°) saline were injected into the spermatic vein catheter and flushed through with an additional 10 μl of warm saline.

Two rats with flowmeters installed (9) and two rats prepared as in Fig. 1b were used to investigate possible molecular transfer of substances from the spermatic artery to the spermatic vein. Tritiated water (25 μCi) was infused into a spermatic vein of these 4 rats over a 12-min period while sequential femoral artery and testis artery samples (20 μl) were drawn at 3-min intervals. Blood

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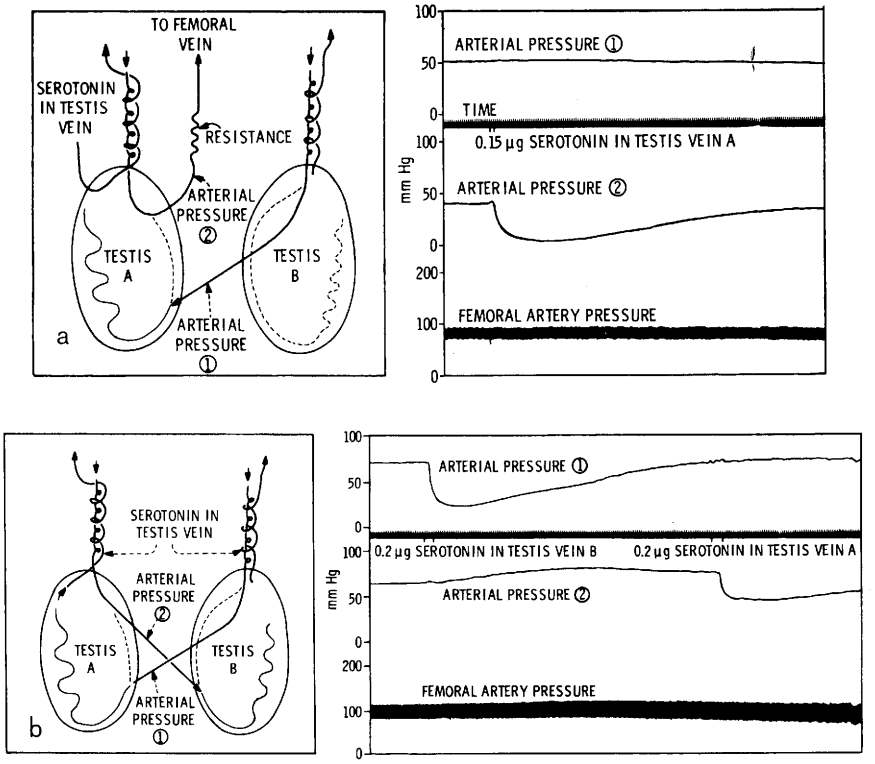

FIG. 1. Localization of the site of venous–arterial interaction of serotonin in the pampiniform plexus of rat. Upward deflections of the time–event scale indicate 5-sec intervals. Downward deflections of the time–event scale occur at the start and completion of each injection. (a) Expt 1: spermatic arterial blood from testis A was shunted through a resistance to the femoral vein while arterial blood from testis B was shunted to testis A. (b) Expt 2: the testes were cross-circulated.

samples were place in 10 ml Aquasol (New England Nuclear, Boston, MA) and counted in a scintillation spectrometer.

Results and Discussion. Control injections of 20 µl warm saline into the spermatic vein had no observable effect on pressure in the testis artery. In 5 rats given 0.3 µg serotonin/kg body weight, lateral pressure in the testis artery was reduced from 64.8 ± 11.9 to 41.2 ± 9.8 mm Hg (64% of pretreatment levels) with no effect on central arterial pressure. The effect was transient, lasting less than 2 min in every case, but was repeatable and could be maintained by infusion.

A dose–response curve of testis artery pressure to serotonin given via the testis vein is shown in Fig. 2. Minimum dose level observed to affect the testis artery pressure was 0.04 µg/kg body weight where 2 µg/kg body weight was the minimum dose required to exert an observable central depressor action. In order to determine if this venous–arterial interaction involving serotonin was mediated via the capillary bed of the testis, serotonin was injected into the spermatic veins of 6 rats in which blood flow through the spermatic vein was made independent of blood flow through the corresponding testis artery. The experimental arrangements and typical results are illustrated in Fig. 1a and b. A decrease in arterial pressure following an intravenous injection of serotonin occurred only in the artery on the same side as the injected vein, demonstrating that this response does not depend on capillary flow between these vessels. Interruption of blood flow in the vasal and epididymal artery of 3 rats did not alter the results, indicating these vascular beds play no role in the phenomenon. Thus, it appeared that the site of interaction is in the

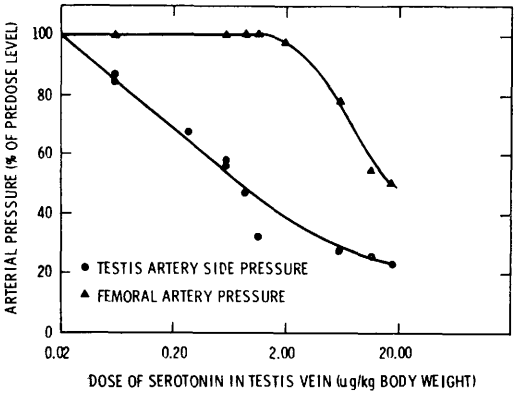

FIG. 2. Dose–response of blood pressure in the femoral and testis artery of rat to serotonin in the testis vein (composite data from 3 rats).

pampiniform plexus.

The tightly coiled testis artery is intimately associated with the spermatic vein in the pampiniform plexus. Possibly, increases in venous pressure or contraction of nonvascular smooth muscle in the pampiniform plexus could increase resistance in the spermatic artery by mechanical compression or by "kinking" of the coils. However, serotonin mildly depressed spermatic vein pressure coincident with the drop in arterial pressure and flow rate (Fig. 3a and b). In contrast, spermatic vein injections of prostaglandin $F_{2\alpha}$ markedly increased spermatic vein pressure and only slightly decreased spermatic artery lateral pressure (2). As the major nonvascular smooth muscles in the spermatic cord are those of the vas deferens, the effect of removal of a 2 cm length of the vas was investigated in 4 rats. Venous–arterial interaction following intravenous serotonin was not affected. Linear displacement of the spermatic cord was measured in 4 rats using an isotonic displacement transducer, demonstrating some relaxation of the cord in response to intravenous serotonin (Fig. 4). The increase in spermatic cord length was unaffected by vas deferens excision and correlated well with changes in spermatic artery lateral pressure. These experiments indicated that the venous–arterial interaction is not significantly influenced by changes in venous pressure or by vas deferens contrac-

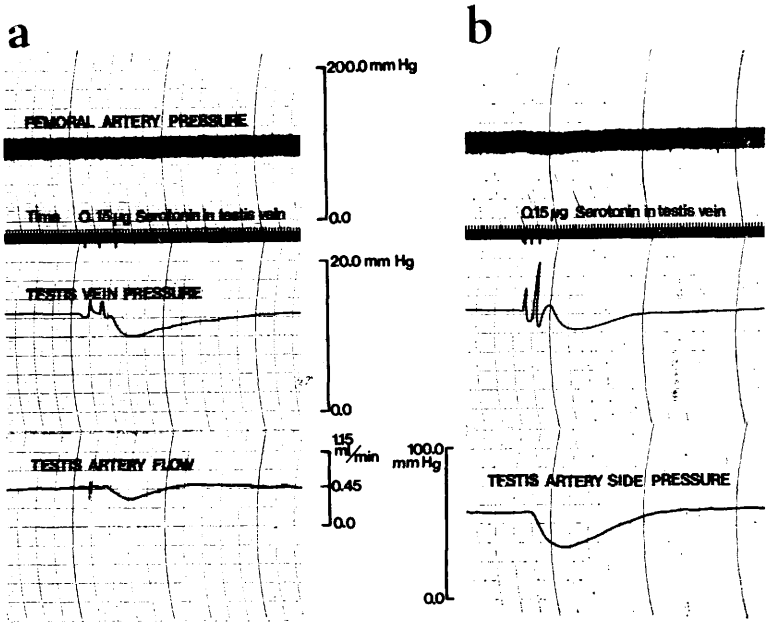

FIG. 3. Effect of serotonin in the testis vein on local blood flow and pressure. Downward deflections of the time–event scale occur at the start and completion of each injection and at the end of flushing. Upward deflections indicate 5-sec intervals. (a) Effect on testis vein pressure and blood flow. Blood flow was monitored using the differential pressure technique described by Jaffe and Free (9). (b) Effect on testis vein and artery blood pressure.

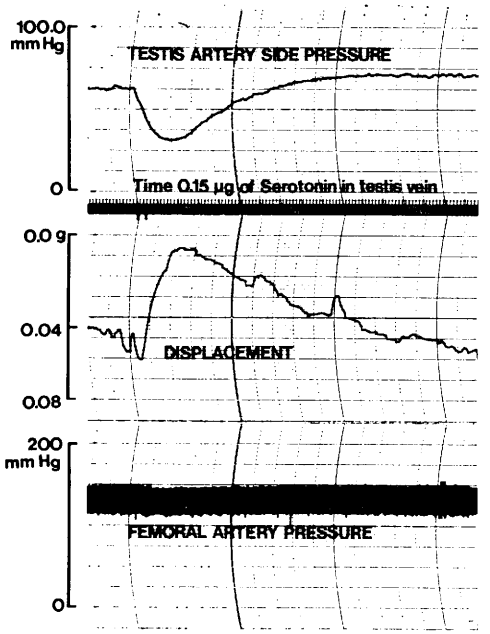

FIG. 4. Effect of serotonin in the testis vein on length of the spermatic cord. Time–event scale as in Fig. 1. Displacement indicates the weight required to cause an equivalent change in the spermatic cord length.

tion.

The major site of serotonin binding in the male reproductive tract has been shown to be the blood vessels of the pampiniform plexus (5), and subcutaneous serotonin (25 mg/kg) is known to cause temporary total occlusion of the proximal testicular artery (7). Experiments were performed to investigate possible molecular transfer of substances from the spermatic vein to the spermatic artery within the pampiniform plexus. Because labeled serotonin shut off the blood supply to the sampling catheters, it was not possible to use this compound. Therefore tritiated water was infused into a spermatic vein of 5 rats while simultaneous femoral artery and testicular artery samples were drawn. Two of the experiments were performed on cross-circulated preparations similar to that illustrated in Fig. 1b to eliminate the possibility of retrograde diffusion. Figure 5 illustrates a typical result which demonstrated that tritiated water can pass easily from the vein to the artery and was present in tenfold higher concentrations in testicular artery blood than in femoral artery blood. These data offer no insight into the movement of serotonin in the pampiniform plexus. However, they do show that molecular transfer can take place between the spermatic vein and artery and add some support to the general conclusion that serotonin from the effluent blood can directly affect the affluent blood supply.

It is possible that the venous–arterial interaction involving serotonin may be more important as an example of a more general functional shunt mechanism of physiological and pharmacological interest than as a physiological control mechanism. However, serotonin in the spermatic vein can bring about a marked constrictor response of the spermatic artery without entering the general circulation, probably by passing directly from vein to artery in the pampiniform plexus. These observations together with the following suggest some regulating role for serotonin in testicular function through control of the affluent blood supply: the high sensitivity and constrictory response of the spermatic artery to serotonin revealed by the present study and others (3, 6, 7) and to endogenous serotonin as revealed by the necessity of antiserotonin for successful testis perfusion [(8) and unpublished data by the authors], the tolerance of the rat testis to ischemia (10), and the restraining effect of the pineal gland on testis and accessory gland weights [see

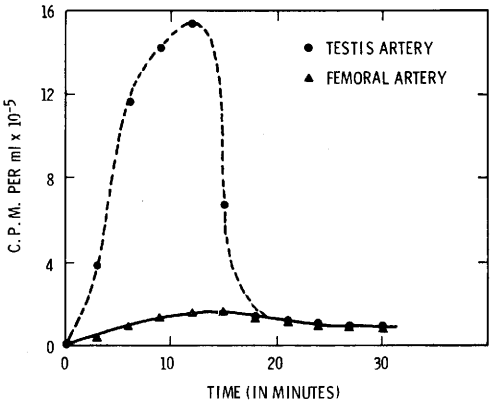

FIG. 5. Radioactivity in blood from the testis and femoral arteries after a 12-min infusion of tritiated water (25 µCi) into the testis vein.

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Summary. Serotonin injected into the spermatic vein had a marked depressor effect on the testis artery at dose levels having no observable effects on central blood pressure. This venous arterial interaction was not dependent on capillary flow between the vein and artery, on flow through the vasal or epididymal artery, on venous pressure or on changes in the vas deferens. Transfer of tritiated water from the spermatic vein to testis artery was demonstrated, indicating that such molecular transfers were possible. It was concluded that serotonin in the spermatic vein can bring about a marked constriction of the testis artery without entering the general circulation, probably by passing directly from the vein to the artery in the pampiniform plexus.

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