The Action of Adrenin on Veins. (*Preliminary Communication.*)

By J. A. Gunn and F. B. Chavasse.

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(From the Pharmacological Laboratory, Oxford.)

It would be remarkable if the vein wall were the only tissue in the body to possess contractile fibres without a functionally important duty of contracting. Very little attention, however, has been paid to physiological alterations in the calibre of the veins, though such alterations may be of high importance in modifying physiological and pathological conditions of the circulation, and in explaining certain actions of drugs.

The following investigation was undertaken in the hope of adding something to the knowledge of the contractile power of the veins; and, though the intended scope of the inquiry has not yet been completed, results have already been obtained which appear to be of sufficient importance to justify their being placed on record.

Method.

The method employed for recording the contractions of veins was similar, in essential respects, to that used by Cow* for determining the reactions of surviving arteries. In our experiments the veins were obtained from freshly killed sheep, and put, as soon as they could be obtained, into a Dewar flask containing oxygenated Ringer's solution at 37° C., and so conveyed to the laboratory.

A large water-bath, kept, unless otherwise stated, with a variation of half a degree on either side, at 36° C., held two beakers containing oxygenated Ringer's solution at the same temperature. In one of these beakers the veins were put until required; in the other was put the part of the vein used for each experiment. For these experiments ring preparations were made. It is difficult to cut quickly and without undue manipulation of the vein a ring of absolutely uniform cylindrical length; but the rings used had a length averaging 1·5 mm., which varied not more than ½ mm. on either side at different parts of the ring. The ring was suspended between platinum hooks, the lower hook being fixed, the upper attached by a silk thread to a lever, which recorded variations in the calibre of the ring upon a slowly revolving drum.

* Cow, 'Journ. Physiol.,' 1911, vol. 42, p. 125.

(a) *Veins Remote from the Heart.*

All the ring preparations of (large) veins which we have so far subjected to the action of adrenin have responded by contraction. In the experiments illustrated in the accompanying figures the magnification of movement was the same in each case. Fig. 1 shows the contraction of an external jugular,

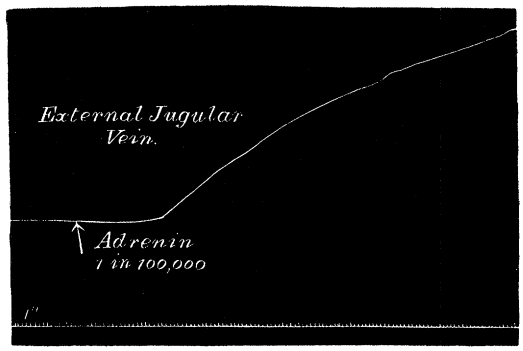

FIG. 1.

fig. 2 of a mesenteric, vein. In regard to the amount of contraction produced they are, however, not comparable, because the temperature in the case of the mesenteric vein was higher (41° C.) than in the other experiments, in which it was 36° C.

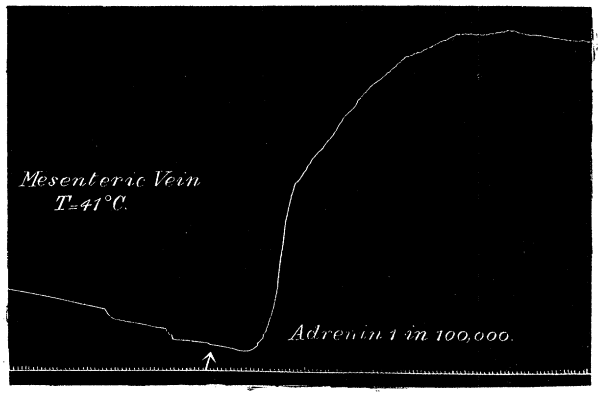

FIG. 2.

The fact that veins contract under the action of adrenin renders it highly probable that veins possess venoconstrictor fibres supplied from the thoracico-lumbar sympathetic system. Several observers have concluded that the portal veins contain venomotor nerves; but the presence of such nerves in other veins rests mainly on the evidence of Thompson* and Bancroft,† who

* Thompson, 'Archiv f. Physiol.,' 1893, p. 102.

† Bancroft, 'Amer. Journ. Physiol.,' 1898, vol. 1, p. 477

found that stimulation of the sciatic nerve in the cat and rabbit produced visible contraction of the superficial veins of the hind limbs.

(b) *Veins Near the Heart.*

Considerable interest attaches to the action of adrenin on the great veins near the heart. It has long been known that in the mammal the great veins near the heart, which correspond in some ways at least to the sinus venosus in the frog, beat rhythmically with the heart proper. One of us has on previous occasions made unsuccessful attempts to obtain a spontaneously contracting ring preparation of the superior vena cava of the cat and rabbit. A renewal of this endeavour with the larger rings from the sheep and bullock has been equally unsuccessful, though it is not suggested that this may not yet be accomplished.

What we believe to be a phenomenon of considerable interest and importance is that such a quiescent ring preparation of the superior vena cava near the heart can be made to beat vigorously and rhythmically by the action of adrenin.

For these experiments the venæ cavæ were removed along with part of the auricle, so that the distance of the ring from the auricle could be measured accurately.

Fig. 3 shows the effect of adrenin, 1 in 20,000, on a ring preparation of the superior vena cava of a sheep, 6 mm. distant from the angle of its junction with the auricle. The kind of effect produced by adrenin on this venous ring is exactly like that produced by it on the whole heart. Though it cannot be postulated with absolute certainty in the case of the quiescent tissue, inspection of the tracing leaves little room for doubt that adrenin augments and accelerates the contractions of the ring.

In the first place, therefore, this method of experiment affords evidence in favour of the view that the augmentor-accelerator nerve supply of the heart extends for some distance up the superior vena cava.

Secondly, it throws some light on the origin of the rhythmicity of the heart. The ring of the superior vena cava is quiescent. (This is established not only by the absence of movements of the lever, but also by observation of the ring in a strong light.) Adrenin almost immediately induces powerful rhythmic contractions. The action of adrenin is a continuous stimulus to which the muscle responds by a discontinuous (rhythmic) contraction.

Now the researches of Lewandowski, Langley, Elliott, Dale, and others have established with an unusual degree of certainty that adrenin acts on the myo-neural junctions of the thoracico-lumbar sympathetic system, and that its action is confined to these. Unless, therefore, the action of adrenin

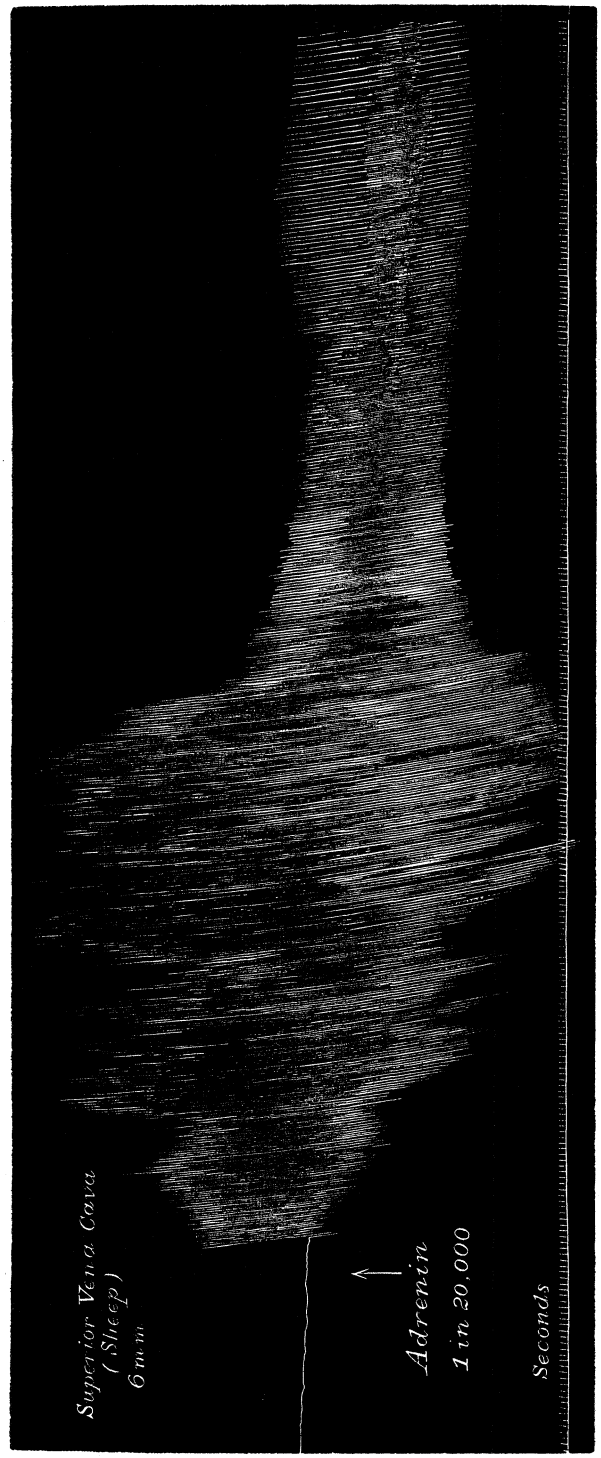

FIG. 3.

on the superior vena cava is unique, there are apparently only two ways in which its action on the quiescent superior vena cava can be explained.

On the neurogenic hypothesis of the rhythmicity of the heart, it is possible to hold that the continuous stimulation by adrenin of the sympathetic myo-neural junctions so raises the excitability of the muscle that previously subminimal rhythmic impulses from intrinsic motor ganglia (hypothetically present in the ring preparation) are now adequate to elicit rhythmic contractions.

On the myogenic hypothesis, on the other hand, stimulation of the myo-neural junctions of the sympathetic nerve causes the muscle to enter into the rhythmic activity which is inherent in it.

All that can be said at present is that the latter explanation seems somewhat more probable. If, however, we should be able to elicit, by adrenin, rhythmic contractions in a ring of the superior vena cava in which subsequent histological investigation can reveal no ganglia, then it would furnish a cogent argument in favour of the myogenic hypothesis of the rhythmicity of the heart.

Further, this kind of investigation has afforded, and with further experiment, it is hoped will afford with greater accuracy, a physiological method of determining how far the rhythmically contractile tissue extends up the great veins, and where it merges into non-rhythmic contractile tissue. The difference in physiological reaction can be controlled by subsequent histological investigation. In the meantime it can be said that the rhythmically contractile tissue extends up the superior vena cava of the sheep for at least

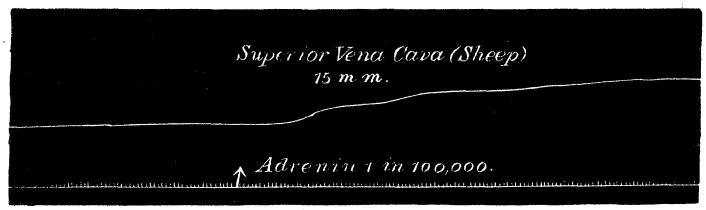

FIG. 4.

6—8 mm. from the veno-auricular junction. Fig. 4 shows that 16 mm. from this junction, a ring of the same superior vena cava which gave the rhythmic contractions shown in fig. 3 responds to adrenin by simple contraction. It must be emphasised that a negative result in inducing rhythmic responses is not in itself conclusive, because, even at 6 mm. distance from the heart, adrenin does not always induce rhythmic contractions. Under the conditions of the present experiments it is not possible for the veins to reach the laboratory always in the same condition of excitability; and we have found

that a negative result is likely to arise when the muscle of the vein is subnormally excitable to electrical stimulation.

In the inferior vena cava we have on no occasion been able to induce rhythmic contractions. The rings of the inferior vena cava have always responded by simple non-rhythmic contraction, as shown in fig. 5.

These experiments are being continued, and extended to the action of other drugs.

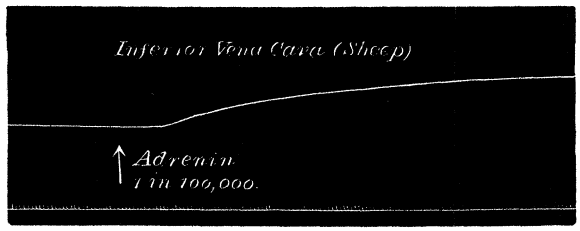

FIG. 5.

Summary.

1. The action of adrenin upon ring preparations of veins remote from the heart is to diminish their calibre, as in the case of arteries. They, therefore, probably contain venoconstrictor nerve fibres from the thoracico-lumbar sympathetic system.

2. The action of adrenin on quiescent rings from the superior vena cava near the heart is to cause them to beat rhythmically and powerfully.

3. (*a*) The accelerator-augmentor nerve supply of the heart, and (*b*) the rhythmically contractile tissue, extend up the superior vena cava for at least 6—8 mm. from the veno-auricular junction in the heart of the sheep.

4. The induction by adrenin of rhythmic contraction in the quiescent superior vena cava seems, on the whole, in accordance with the myogenic theory of mammalian heart rhythmicity.