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THE SYMPATHETIC DILATOR FIBRES IN THE MUSCLES OF THE CAT AND DOG.

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In an earlier communication one of us [Burn, 1932] has described the occurrence of vaso-dilatation in the perfused hind limbs of the dog when the sympathetic chain is stimulated. Defibrinated blood was perfused by means of a Dale-Schuster pump [1928] through the abdominal aorta, and collected again for reoxygenation from the inferior vena cava. Under these conditions the tone in the vessels was very low, and stimulation of the sympathetic chain had little or no effect. When adrenaline was added at a constant rate to the venous reservoir, so that the tone in the vessels became higher, stimulation of the sympathetic chain then often produced a vaso-dilatation, more especially when a relatively strong stimulus was applied for a short time. In some experiments vaso-constriction was never observed.

Since these results were published, further observations showed that vaso-dilator effects of the kind described were not seen in cats. This difference between the two species brought to mind a similar difference in their behaviour towards histamine. Dale and Richards [1918] were able to find conditions in which a vaso-dilatation could be observed to follow the injection of histamine in the perfused vessels of the cat, but this dilatation was much more difficult to evoke than in the dog, in which Burn and Dale [1926] found that histamine regularly caused vaso-dilatation. Moreover, both the dilator action of histamine in the perfused vessels of the cat and the dilator effect of sympathetic stimulation in the perfused vessels of the dog were most readily seen when adrenaline was added to the perfusion fluid.

PERFUSION EXPERIMENTS.

Experiments were therefore performed to see whether the two dilator effects were similarly affected by different conditions of tone. The dilator action of acetylcholine was examined at the same time, but it was expected that the action of this substance would be unaffected by different conditions of tone since it is readily displayed in the vessels of the cat perfused with Ringer's solution.

METHOD.

The method of perfusion with the Dale-Schuster pump has already been described [see Burn, 1932]. The viscera were removed, and bleeding from the muscles of the body wall was prevented by mass ligatures. The arterial cannula, from a side tube in which the pressure was recorded, was inserted in the abdominal aorta just below the renal arteries, and the blood was collected from the vena cava at a similar level.

When it was desired to raise the tone with adrenaline, a 1 in 40,000 solution in saline was allowed to drop from a burette into the reservoir collecting the venous blood. This blood was pumped through the lungs and then again to the legs. A tone with pituitary extract was obtained by adding to the venous reservoir amounts equal to 5 units at intervals; for example, a total of 30 units might be added, the total blood in circulation being usually 600 c.c.

EXPERIMENTAL RESULTS.

(*a*) *Dilator effect of acetylcholine.*

The dilator action of histamine was found to be increased in those circumstances in which the dilator effect of sympathetic stimulation was increased; in this point the result agreed with what was expected; there was, however, a similar change in the dilator action of acetylcholine. Thus, when the dilator effect was examined in vessels in which the tone was maintained by pituitary extract and then later in the same vessels when the same degree of tone was maintained by adrenaline, the dilator effect of acetylcholine was greater in the presence of adrenaline (see Fig. 1).

(*b*) *Cholinergic mechanism.*

In some of these experiments in which the hind limbs were perfused, the skin was first removed. The dilator effects of sympathetic stimulation were even more easily seen than before; indeed a constrictor response of

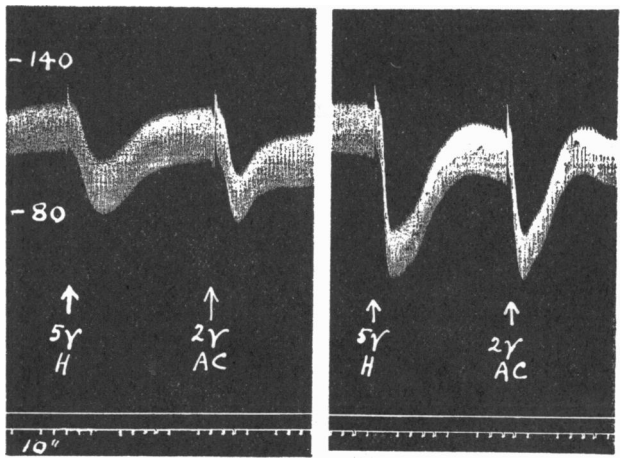

Fig. 1. Record of the changes in perfusion pressure when the vessels of the hind limbs of a dog are perfused with defibrinated blood. On the left are the dilator effects of 5γ histamine and of 2γ acetylcholine when the tone was maintained with pituitary extract; on the right are the dilator effects of the same substances when the tone was maintained with adrenaline.

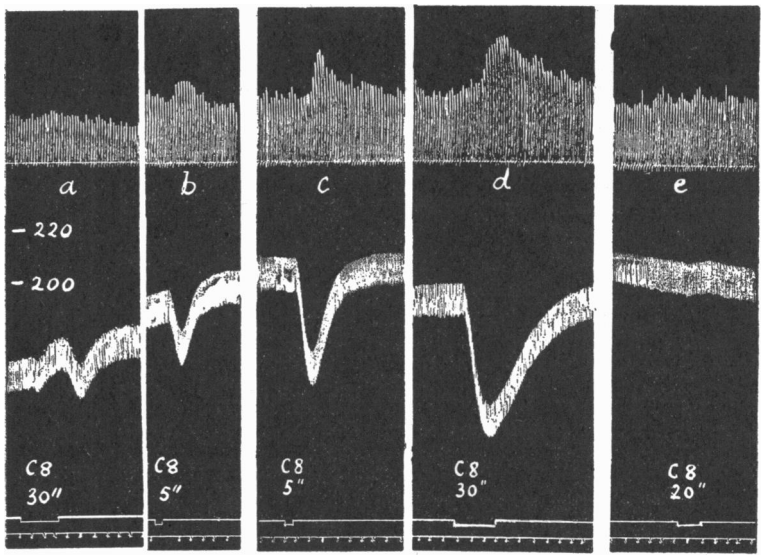

Fig. 2. Perfusion of dog's hind legs as in Fig. 1. *a* and *b* show the effect of stimulating the left sympathetic chain for 30 sec. and 5 sec. respectively. 12 mg. eserine was then added to the perfusing blood. *c* and *d* show the much greater dilator effects obtained on stimulating for 5 sec. and 30 sec. 2 mg. atropine was then injected into the vessels. Stimulation (*e*) is then ineffective. At the top the outflow is recorded by Gaddum's recorder.

the vessels was rarely observed. Sir Henry Dale suggested to us at this point that we should examine the possibility that the dilator effect of sympathetic stimulation was produced in the muscles by the liberation of acetylcholine at the nerve endings; he thought that the fibres concerned might belong to the class he has called "cholinergic" [Dale, 1933].

Other perfusion experiments were therefore performed in which the response to stimulation was observed before and after the addition of eserine to the perfusing blood. A portion of the sympathetic chain of one side was enclosed in fluid electrodes of the pattern described by Brown

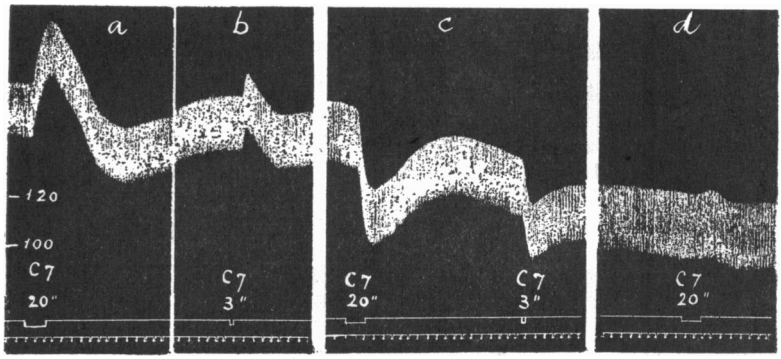

Fig. 3. Experiment as in Fig. 2, showing constrictor effects in skinned legs of stimulating the sympathetic chain for 20 sec. and 3 sec. respectively (*a* and *b*). 5 mg. eserine was then added. Stimulation for 20 sec. and 3 sec. (*c*) now caused dilatation. After 5 mg. atropine was given, the stimulation (*d*) produced a slight constriction.

and Garry [1932] and break shocks at the rate of 16 per second were applied. In some experiments the venous outflow was recorded by means of Gaddum's recorder [1929]. Fig. 2*a* and *b* shows the effect of stimulation for a long and a short period respectively, before the addition of eserine. As previously described [Burn, 1932] the stimulus when applied for a short time gives a simple dilator response, whereas the longer stimulus gives a response which is a mixture of dilatation and simultaneous constriction. Eserine was then added to the perfusing blood in part by way of the arterial cannula and in part by way of the venous reservoir, up to a total of 12 mg. Repetition of the short stimulation then gave a greater dilatation than before, while repetition of the long stimulation was followed by a large fall of blood-pressure instead of by the previous indefinite variation. The final portion of the figure (Fig. 2*e*)

illustrates the abolition of all dilator effect after the injection of 2 mg. atropine. In Fig. 3 is the record of another experiment in which the initial response to stimulation was constrictor, while after the addition of eserine the response was dilator. Both experiments make it clear that the dilator component of the response to sympathetic stimulation is magnified in the presence of eserine and subsequently abolished by atropine.

(*c*) *Experiments on the leech preparation.*

Since these results indicated that the dilator effect was due to the liberation of acetylcholine, attempts were made to obtain evidence of the presence of this substance in the venous perfusate. The hind limbs

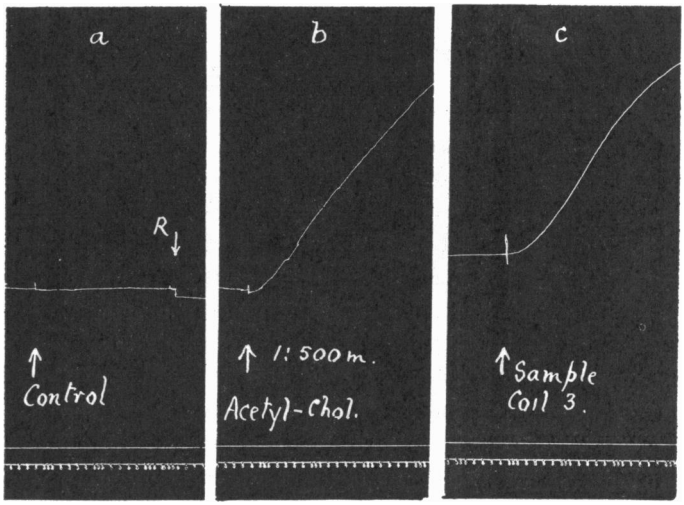

Fig. 4. Leech preparation; the figure shows the effect of applying a sample of the venous perfusate coming from the hind limbs of a dog (after removal of the skin); *a*, without stimulation; *c*, during stimulation of the sympathetic chain. The contraction produced in *c* is about equivalent to 1 in 500 millions acetylcholine (*b*).

of a series of dogs were perfused with Ringer's solution containing eserine in concentration 1 in 400,000 and adrenaline 1 in 200,000. Samples of fluid coming from the cannula in the vena cava were then tested on the preparation of leech muscle described by Führer [1918] and modified by Minz [1932]. Each sample of 5 c.c. was transferred on withdrawal to a small graduated cylinder standing in a mixture of ice and salt, and 2 c.c. of a 1 in 400,000 solution of eserine in distilled water was added.

The sample was thus kept until it was tested; before being tested it was rapidly warmed to room temperature. During the perfusion with Ringer's solution it was still possible to observe a small dilator effect after stimulation of the lumbar sympathetic chain during the first 15–30 min. Samples taken when this dilator effect was seen were found to have a stimulant action on the leech muscle corresponding to concentrations of acetylcholine of from 1 in 500 to 1 in 100 millions. An example taken from an experiment in which the skin was removed from the legs is given in Fig. 4. The amounts of acetylcholine thus detected were too small to verify by other tests.

Experiments on anæsthetized dogs.

The relation of effects observed in blood vessels perfused by means of a mechanical pump to effects produced in the living body is quite uncertain, and it remained to discover whether dilator responses to sympathetic stimulation could be observed in the muscles of the anæsthetized dog. Schneider [1934] has shown that when the Thermostromuhr devised by Rein is applied to the femoral artery immediately below Poupart's ligament, and the peripheral end of the sympathetic chain is stimulated, the rate of blood flow may rise from 69 to 180 c.c. per minute, from which he concludes that vaso-dilator fibres run in the sympathetic chain to the hind limbs. Our own observations were made on dogs prepared by injecting pernocton (a derivative of barbituric acid) into the muscles using a dose of 0·5 c.c. per kg. as recommended by Rein and Schneider [1934]. The dogs were eviscerated, and a plethysmograph was applied to one leg after removing the skin together with the foot, which was disarticulated at the lower end of the tibia. The plethysmograph was of the pattern described by Ranson and Wightman [1922] consisting of a metal outer case, oval in cross-section, and tapered towards one end. A rubber stocking to fit the leg of the dog is fastened over the larger open end. The stocking is fitted over the leg, and the space between the stocking and the metal case is filled with warm water. In our experience this pattern of plethysmograph is easy to apply, and gives good records when attached to a piston recorder.

(*a*) *Observations after injection of eserine.*

The results of the application of stimuli to the sympathetic chain are conveniently shown in Fig. 5. A stimulus lasting 10 sec., and also a stronger stimulus for 3 sec., both caused constriction in the muscles,

though that produced by the short stimulus was very slight. Eserine was then injected intravenously in a series of small doses to a total of 0·8 mg., and the stimuli were repeated about 10 min. after the last injection of eserine. The short stimuli now produced vaso-dilatation accompanied by a fall in the blood-pressure, while the weaker stimulus

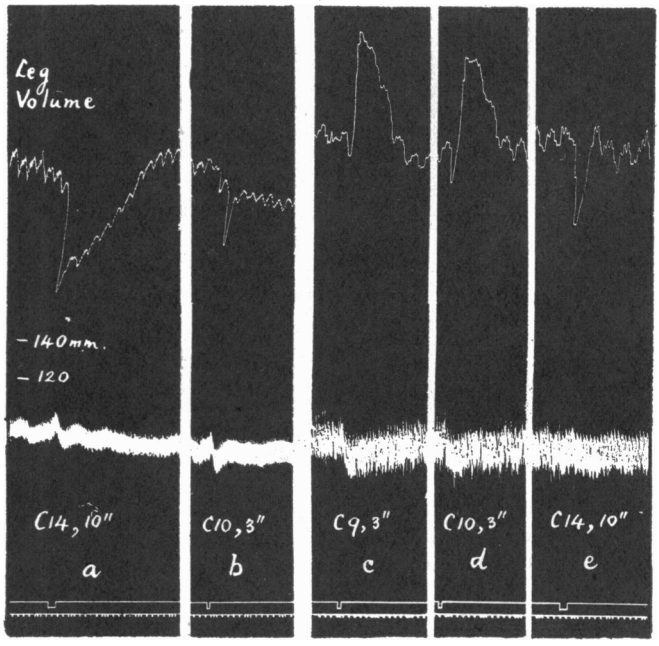

Fig. 5. Dog anæsthetized with pernocton. Upper record is volume of left hind limb (skin removed). Downstroke is constriction. *a* and *b* show constriction when sympathetic chain was stimulated. 0·8 mg. eserine was then injected. *c* and *d* show the dilator effect of stimulating for 3 sec. *e* shows the constrictor effect of a longer stimulus though less than in *a*.

applied for a longer time still produced vaso-constriction. The total dose of eserine in different experiments varied from 0·1 to 0·3 mg. per kg. The effect of injecting atropine is shown in Fig. 6, in which it is seen that the dilator response produced by stimulation for 3 sec. with the secondary coil at 9 cm. in the presence of eserine was replaced by a constrictor response; the constrictor response after atropine, it may be noted, was greater than the constrictor response seen in Fig. 5 before eserine was injected.

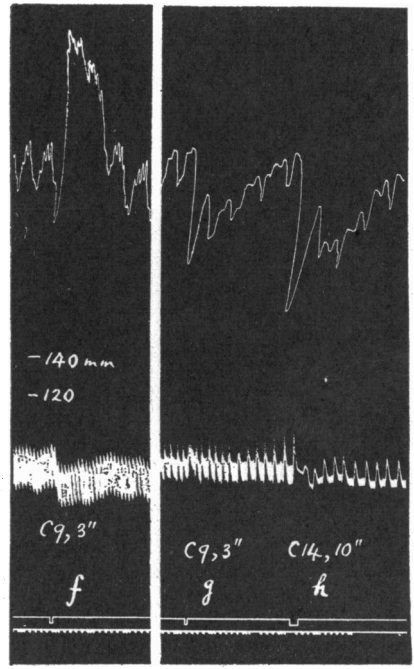

Fig. 6. Same experiment as Fig. 5. The dilator effect in *f* is converted by the injection of atropine into a constrictor effect *g*, which is now a greater constriction than was observed in *b*. Similarly the constrictor effect *h* is greater than that in *e*, and about the same as *a*.

(*b*) *Observations after the injection of ergotoxine.*

This vaso-dilatation revealed by eserine, evidently cholinergic, at once suggested that the dilatation obtained after the injection of ergotoxine should be examined. We are unaware whether it has previously been shown that stimulation of the sympathetic chain after the injection of ergotoxine is followed by vaso-dilatation in the muscles of the dog, but actually we have found that it is very readily observed either in the spinal dog or in the dog anæsthetized with pernocton. Much larger doses of ergotoxine are necessary to produce the reversal of the pressor effect of adrenaline than in the cat in which 0·5 mg. per kg. is usually enough. A dose from 1·0 to 5·0 mg. per kg. is needed in the dog, but the vaso-dilator effect of sympathetic stimulation is seen after 0·5–1·0 mg. per kg. In a series of experiments the results were uniform and indicated that the dilatation produced after ergotoxine by sympathetic stimulation was

cholinergic. Fig. 7 shows the dilatation obtained by stimulation after 9·0 mg. ergotoxine; this was increased after the injection of 0·4 mg. eserine and still further increased by 0·2 mg. in addition. The injection of atropine abolished the dilator effect.

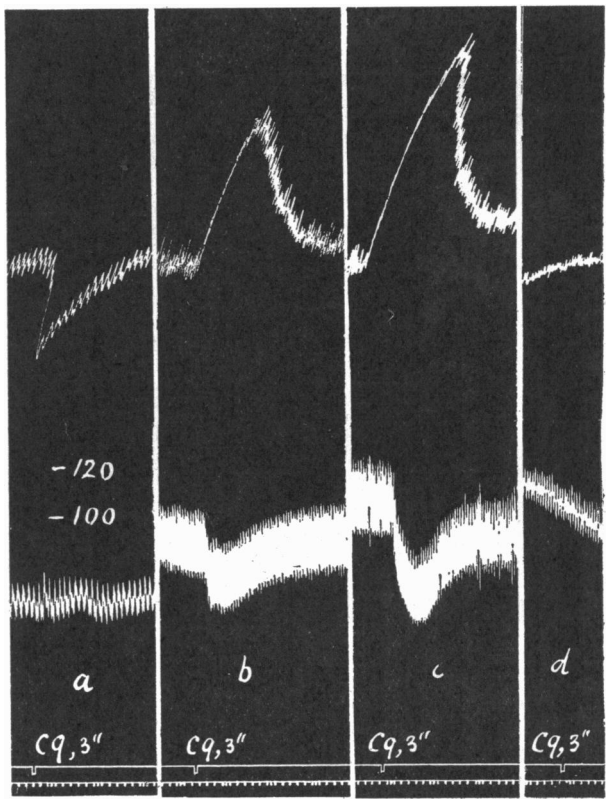

Fig. 7. Dog anæsthetized with pernocton. Upper tracing is volume of skinned leg. *a* shows constriction produced by stimulation of sympathetic chain; *b* shows dilatation after 34 mg. ergotoxine, and *c* the increased dilatation after 0·9 mg. eserine. *d* shows the abolition of the dilator effect by atropine.

(*c*) *Adrenaline vaso-dilatation.*

Fig. 8 illustrates the observation that although atropine abolishes the dilatation produced after ergotoxine by stimulation of the chain, it does not affect in any way the dilatation produced by adrenaline. In this experiment a total of 50 mg. ergotoxine was injected to produce the full adrenaline reversal on a dog of 10 kg.

In addition to the vaso-dilatation produced by adrenaline after ergotoxine, there is also the vaso-dilatation produced by small doses of adrenaline in dogs anæsthetized with ether. We examined this vaso-dilator effect in a dog prepared by section of the sciatic and anterior

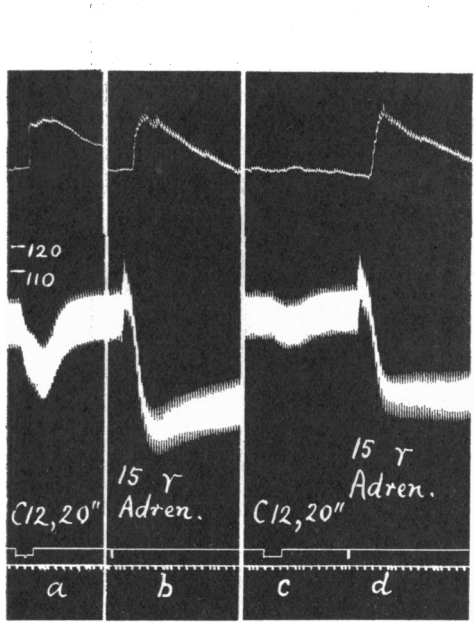

Fig. 8.

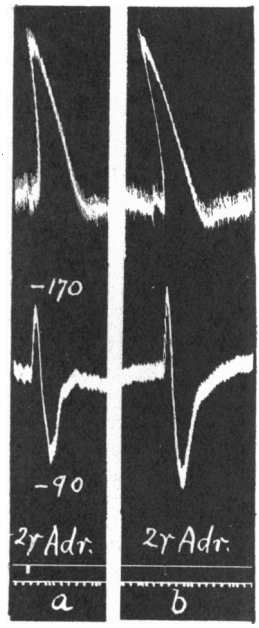

Fig. 9.

Fig. 8. Dilator effects after 48 mg. ergotoxine; *a* due to stimulation, *b* to 15γ adrenaline. 2·0 mg. atropine was then injected after which stimulation (*c*) no longer produces dilatation, but adrenaline (*d*) does so as before.

Fig. 9. Dilator effects in dog anæsthetized with ether; vagi cut. Upper tracing is volume of fully denervated leg after removal of skin. *a* shows dilator effect before and *b* shows the same effect after 2·0 mg. atropine.

crural nerves of one side. The nerve sections were carried out three days before with full aseptic precautions. The dog was anæsthetized with ether, the vagi were cut, and a plethysmograph record of the leg of the operated side was taken after removal of the skin. When 2γ adrenaline was injected intravenously there was a prompt expansion of the limb volume accompanied by a fall of blood-pressure. This vaso-dilator action was completely unaffected by the injection of atropine as shown in Fig. 9.

(d) Vaso-dilatation after the infusion of adrenaline.

The vaso-dilator effect of sympathetic stimulation had been obtained so far only by the use of eserine and ergotoxine which are not normal constituents of body fluids. In the perfused preparation, the addition of adrenaline had revealed vaso-dilatation, and we therefore carried out

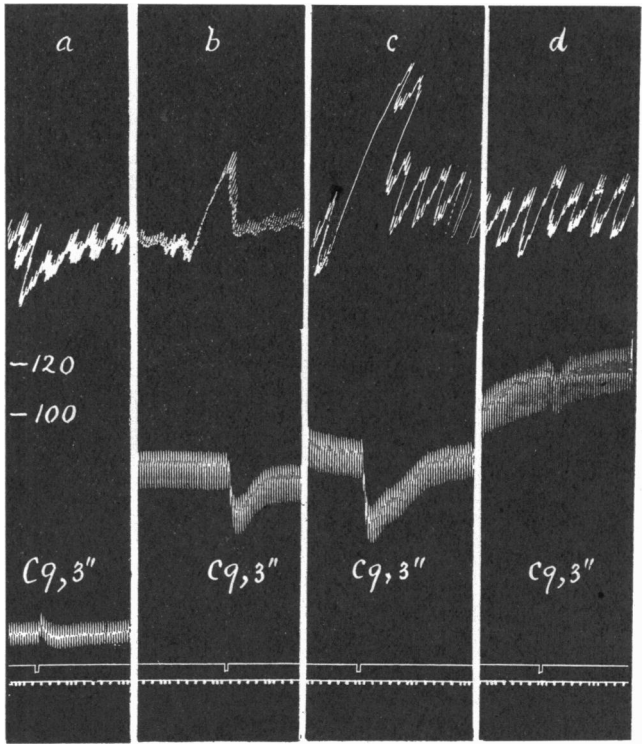

Fig. 10. Dog, pernocton. Volume of skinned limb. *a*, constrictor effect of stimulation of sympathetic chain; *b*, dilator effect of the same stimulation during the infusion of adrenaline into a vein; *c*, increased dilator effect after 0·6 mg. eserine; *d*, abolition of dilator effect after 4 mg. atropine.

experiments to see whether adrenaline had the same action in the anæsthetized animal. Having prepared the eviscerated animal as before, we proceeded to infuse into the external jugular vein a 1 in 100,000 solution of adrenaline. We found, as is shown in Fig. 10, that a constrictor response obtained in the muscles before the infusion began, became afterwards a dilator response. Here also the dilatation was

greater after the injection of eserine, and as a rule it was abolished by atropine. The effect of atropine was not however so regular and so decisive as in previous experiments in which eserine or ergotoxine were used; in one experiment the injection of 2·0 mg. atropine did not affect the dilator response, though the subsequent injection of 6·0 mg. greatly reduced it.

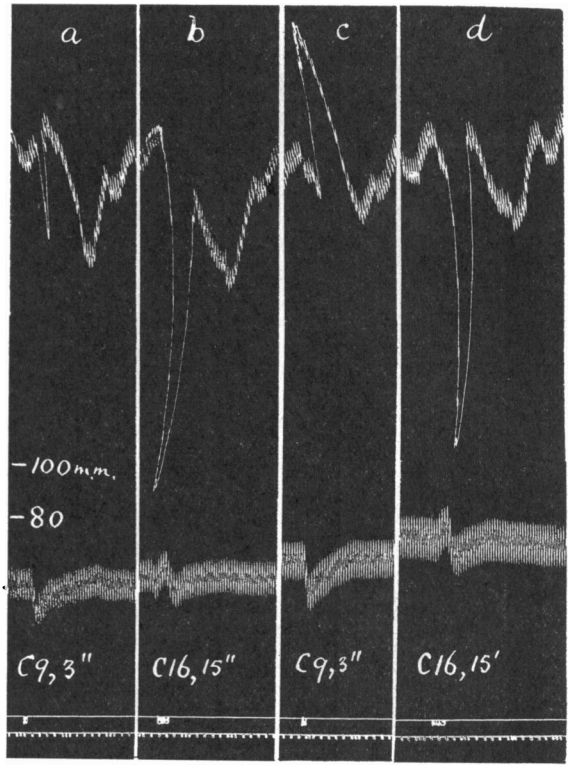

Fig. 11. Dog, pernocton. Volume of skinned limb. *a* and *b*, constrictor effect of short and long stimulation of sympathetic chain during infusion of pituitary extract; *c*, dilator effect of short stimulation during infusion of adrenaline; *d*, constrictor effect of long stimulation during infusion of adrenaline.

(*e*) *The infusion of pituitary extract.*

The action of adrenaline in converting the constrictor response to stimulation into a dilator response seemed most simply explained by supposing that adrenaline produced constriction in the vessels. In constricted vessels the effect of simultaneous stimulation of constrictor and

dilator fibres would be to produce dilatation rather than constriction. We hoped to be able to test this point by infusing pituitary extract instead of adrenaline. The solution of pituitary extract contained 0·4 unit per c.c. We found that the effect differed in different experiments; in one the constrictor response to stimulation was converted to a dilator response, though the dilatation obtained was not so great as when the tone was subsequently maintained by adrenaline. In a second experiment the result of increasing the tone with pituitary extract was that sympathetic stimulation produced mainly constriction, though once when the tone had fallen and the chain had not recently been stimulated, a dilator effect was seen; subsequently a dilator effect was regularly obtained with an adrenaline tone. In a third experiment, dilatation was not obtained during the pituitary tone. Thus it is difficult to give a simple answer to the question whether adrenaline causes the dilator response to appear by constricting the arteries and in no other way. We are of opinion that adrenaline has some specific effect not shared by pituitary extract, of which the record given in Fig. 11 is an illustration.

Effects in the cat.

As was mentioned earlier, dilator effects following sympathetic stimulation have never been observed in experiments in which the hind limbs of the cat were perfused by the Dale-Schuster pump. Having discovered that the dilator effects in the dog were due to the liberation of acetylcholine, we were reminded of one condition in which the muscles of the hind limbs of the cat are known to become sensitive to that substance, namely after section of the motor and sensory roots between the posterior root ganglia and the spinal cord. Sherrington [1894] showed that, two to three weeks after the operation is performed, stimulation of the peroneal nerve causes contracture of the muscles. Hinsey and Cutting [1933] have recently stated that this contracture is due to the stimulation of the sympathetic fibres in the trunk, since they found that stimulation of the grey rami produced the phenomenon. Now if the phenomenon is due to the liberation of acetylcholine and produced by stimulating sympathetic fibres, we thought it might be possible to observe vaso-dilatation in muscles sensitized in the manner described. We prepared a series of cats by dividing the spinal roots on one side from the fifth lumbar to the second sacral root inclusive. Three weeks after the operation the cat was prepared for perfusion through the abdominal aorta, and the gastrocnemius muscle of the operated side was detached

from the os calcis and arranged to pull on a tension lever. A steel rod transfixed the lower end of the femur to hold the leg rigid. The muscle was now found to be sensitive to the injection of acetylcholine, and to

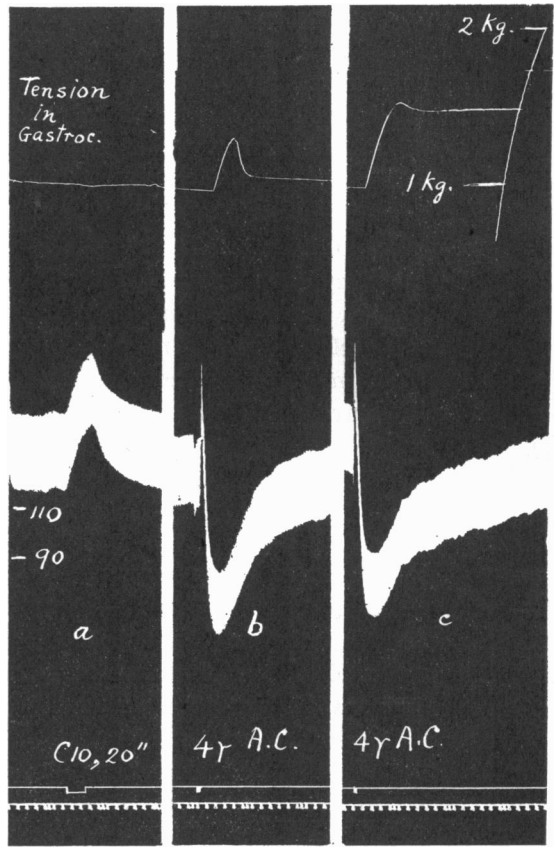

Fig. 12. Perfusion of hind limbs of cat through abdominal aorta. One hind limb denervated 3 weeks previously by section of fifth, sixth, seventh lumbar, and first and second sacral roots. Upper record is tension of gastrocnemius of denervated limb. Stimulation of sympathetic chain caused vaso-constriction but no effect on tension. Injection 4γ acetylcholine in *b* and *c* causes increased tension and vaso-dilatation. Between *b* and *c* 1 mg. eserine was injected.

respond by contracture as shown in Fig. 12, but stimulation of the lumbar sympathetic chain produced only vaso-constriction. The dose of acetylcholine injected in Fig. 12 was 4γ. This is, of course, large, but it is to be remembered that a steady concentration of adrenaline was present

in the perfusing blood. After addition of eserine, the injection of acetylcholine was followed by a prolonged development of tension, as shown in the figure.

Experiments with eserine and ergotoxine.

We have attempted to produce a dilator response in the leg muscles to sympathetic stimulation by injecting eserine into the cat anæsthetized with pernocton. We found, however, that the constrictor response was not affected either by the eserine or by the subsequent injection of

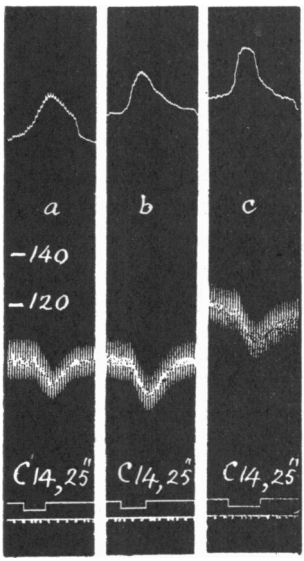

Fig. 13.

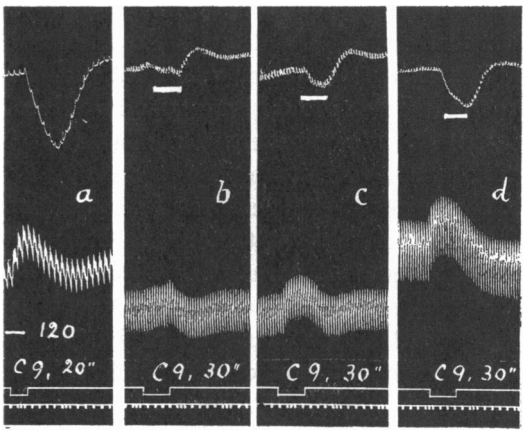

Fig. 14.

Fig. 13. Dilator effect of sympathetic stimulation in muscles of spinal cat after injection of ergotoxine. *b*, after eserine; *c*, after atropine. The injection of these drugs had no effect.

Fig. 14. *a*, constrictor effect of sympathetic stimulation in muscles of cat (pernocton). *b*, unusual result of stimulation during the infusion of adrenaline and after the injection of 1·2 mg. eserine; when the stimulation ceased a slight dilator effect was seen; *c*, a repetition of *b* with less dilatation; *d*, after 2·0 mg. atropine no dilatation.

atropine. Similarly we have examined the dilator response obtained when ergotoxine is injected, but again this dilatation is not increased by eserine or reduced by atropine. The difference between the cat and the dog in this respect is well shown by comparing Fig. 7 with Fig. 13.

Experiments with infusion of adrenaline.

When adrenaline is infused into the external jugular vein, stimulation of the sympathetic chain failed to produce dilatation. In one experiment, however, after eserine had also been injected, a slight dilator effect was obtained (see Fig. 14). The dilatation could not be shown repeatedly, but after the injection of atropine the response became constrictor. We are of opinion that in this experiment there was evidence of the presence of a small cholinergic dilatation.

Discussion.

The experiments leave no doubt that the sympathetic innervation of the blood vessels of the muscles of the dog is not only constrictor, but also has an easily demonstrated dilator component. The dilator fibres act in the main by the liberation of acetylcholine. Curiously enough, cholinergic dilator fibres are absent in the cat, and the few dilator fibres which are revealed by ergotoxine appear to be adrenergic, since they are unaffected by eserine and atropine. The dilator fibres in the dog may be demonstrated not only by the use of eserine and ergotoxine, but by the more physiologically significant use of adrenaline. When adrenaline is infused into a vein at a constant rate, strong stimuli of short duration cause vaso-dilatation. A purely constrictor nerve supply to muscle blood vessels has always been difficult to understand, since in times of stress when the sympathetic system is fully active, the blood supply to the muscles requires to be increased, rather than diminished. Animals like the dog which are capable of more prolonged exertion than the cat, may have this greater capacity because of the presence of the dilator innervation. Why, however, should this dilator innervation be cholinergic rather than adrenergic? Why should the mechanism of the dilatation be completely changed in the two species? An answer to this is suggested if we consider the disadvantages of adrenergic dilator fibres running to the blood vessels in muscle. Efficient working of these fibres will be of most importance to the body as a whole in times of emergency. Yet at these times there is an output of adrenaline from the suprarenal glands which creates a high vascular tone. The small amounts of adrenaline liberated by the dilator fibres must then exert their dilator effect in opposition to this adrenaline tone.

At first sight this seems an impossible task, but various observations have led Dale and Richards [1918] and Burn and Dale [1926] to consider whether adrenaline plays such a double part. We can state from

our own observations that small doses of adrenaline have no vaso-dilator effect whatever in the perfused vessels of the dog's muscles when the tone is maintained by adrenaline, at a time when sympathetic vaso-dilatation is readily produced. We therefore suggest that in the course of evolution the adrenergic dilator mechanism to the muscles has been abandoned because it was necessarily inefficient. Obviously dilator fibres liberating acetylcholine are much more efficient. Acetylcholine has a dilator action which, as we have shown in these experiments, is actually enhanced by an adrenaline tone.

The persistence of the vaso-dilator action of adrenaline in the muscles of the dog is a matter of great interest. Since the vaso-dilator nerves are no longer adrenergic as in the cat, the dilator effect of adrenaline might have disappeared, there being no corresponding innervation. But it has not done so, and its position appears to be similar to that of the dilator effect of acetylcholine in the cat which also corresponds to no known innervation.

While the broad difference between the species is clear enough, we should qualify it by stating that our experiments indicate that it is not absolute. We have found one dog in which the dilator effect of stimulation was not abolished by a small dose of atropine (though larger doses abolished it), and there are some cats in which small dilator effects are seen which appear to be slightly increased by eserine and diminished by atropine. Since Hinsey and Cutting [1933] state that the Sherrington phenomenon can be elicited by stimulating the grey rami, then cholinergic sympathetic fibres must surely be present in some cats.

In conclusion we may point out that our observations throw further light on the action of ergotoxine. Dale [1906] found that a sympathetic innervation which was purely motor was paralysed but not reversed by ergotoxine, while one which was purely inhibitor was unaffected; he, therefore, supposed that the reversal of the pressor effect of adrenaline by ergotoxine was due to the paralysis of motor nerve endings so that the stimulation of the inhibitor endings was no longer masked. Others have doubted this view and thought that ergotoxine might reverse the action of the vaso-constrictor fibres. We now find that the injection of eserine or the infusion of adrenaline in the dog will convert a constrictor response to sympathetic stimulation into a dilator response, just as the injection of ergotoxine does. Since the action of eserine and adrenaline is certainly not to reverse the function of constrictor fibres, it is superfluous to suppose that ergotoxine does so.

SUMMARY.

1. The dilator effect of stimulating the sympathetic chain has been studied when the muscles of the hind limbs of the dog are perfused with defibrinated blood containing adrenaline. The dilator effect is intensified by eserine and abolished by atropine.

2. When the perfusion is carried out with Ringer's solution containing eserine and adrenaline, a substance appears in the perfusate during stimulation which causes contraction of the leech preparation.

3. The effect of stimulating the sympathetic chain has been studied in dogs under pernocton, the volume of the muscles of the hind leg being recorded in a plethysmograph. Sympathetic stimulation causes vaso-constriction.

4. After the injection of eserine, short stimuli (3 sec.) cause vaso-dilatation. This vaso-dilatation is abolished by atropine.

5. After the injection of ergotoxine, stimulation causes vaso-dilatation, and this vaso-dilatation is increased by eserine and abolished by atropine. The vaso-dilator effect of adrenaline after ergotoxine is not affected by atropine.

6. The vaso-dilator effect of small doses of adrenaline in the muscles of the dog anæsthetized with ether is not affected by atropine.

7. During the infusion of adrenaline into the dog under pernocton, short stimuli cause vaso-dilatation. This dilatation is increased by eserine and usually abolished by atropine.

8. During the infusion of pituitary extract, short stimuli sometimes cause vaso-dilatation, but not with the regularity of an infusion of adrenaline.

9. After the injection of ergotoxine into the cat, stimulation causes vaso-dilatation, but this is not increased by eserine and not abolished by atropine.

10. Neither the injection of eserine nor the infusion of adrenaline into the cat lead to the appearance of dilator sympathetic responses, though occasionally when the two are used together, slight dilator effects are obtained.

11. We conclude that there are many cholinergic vaso-dilator fibres in the sympathetic nerve supply of the muscles of the dog. In the cat the sympathetic vaso-dilator fibres appear to be few and in function adrenergic; they can be clearly demonstrated only after the injection of ergotoxine.

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