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VASCULAR REACTIONS OF THE CAT AFTER TOTAL SYMPATHECTOMY

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THE means whereby an animal deprived of its sympathetic ganglionic chains maintains its vascular tone is still unknown, and there is considerable difference of opinion on the existence of vascular reflexes and the means by which they are mediated in such animals. Bacq, Brouha & Heymans [1934] believe that in the sympathectomized cat vaso-motor nerves, which do not pass through the sympathetic chains, control the vascular reactions of the splanchnic area and maintain the tone of the vessels. Rosenblueth & Cannon [1934] and Pinkston, Partington & Rosenblueth [1936], on the other hand, contend that the dilator fibres in the dorsal spinal roots are probably the efferent paths for the blood-pressure changes which occur in completely sympathectomized cats. All these investigators have insisted on the persistence after sympathectomy of centrally controlled vaso-motor nerves maintaining connexion with the blood vessels. Our own experiments on cats give some support to this conception, but we have been able to demonstrate that many of the vascular reactions, which occur in these animals, can be adequately explained on other grounds.

METHODS

The majority of the operations have been done on female cats weighing between 2 and 3 kg. After subcutaneous injection of 1 mg. of atropine, they were anaesthetized with ether, and a tube was passed between the vocal cords into the trachea, and artificial respiration was started from a pump, with a mixture of air and sufficient ether vapour to maintain anaesthesia. No elaborate preparation of the skin was found necessary, beyond shaving and swabbing with 0·1 % mercuric chloride

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solution. Iodine should not be used for the cat's skin, as it sets up irritation of the wound edges, leading to secondary infection [cf. Liddell & Carleton, 1936]. Our operative technique followed more or less closely that of Cannon, Newton, Bright, Menkin & Moore [1929], with some minor modifications. The most satisfactory procedure in our hands has been the removal at one operation of the whole right sympathetic chain, from and including the stellate ganglion, to the pelvis, together with the abdominal sympathetic chain of the left side from the pelvis to the second lumbar ganglion, the right suprarenal gland being removed also at this first stage. After the cat had recovered from this operation, and had regained its normal weight, the left thoracic chain and the remains of the left upper abdominal chain were removed. In our earlier experiments, at a third operation the remaining, denervated, suprarenal gland was exposed, split along its long axis and the medullary tissue scraped out with a sharp spoon. To ensure more complete destruction of the medulla, the exposed surfaces were touched with a crystal of chromic acid before suturing and returning the gland to its bed. In later experiments, we abandoned this procedure as an unnecessary elaboration, and removed the remaining suprarenal at the time of the final experiment. In point of fact, the presence or absence of the denervated suprarenal has made no detectable difference to our results. In four animals, at the second operation, the semilunar ganglia were excised, and again it may be noted that the reactions of these animals were not different from those of animals in which the ganglia were intact. Miss C. J. Hill has examined histologically portions of the small intestine from three of the cats in which the semilunar ganglion had been excised, and informs us that they contain no sympathetic nerve fibres. The final experiment was done as soon as the cat had recovered completely from the last operation, but in no case earlier than 1 week, or later than 3 weeks after operation. In all cats, except one, the weight at experiment was equal to or greater than the weight before the first operation.

For the final experiment, the cats were anaesthetized with ether and the blood pressure recorded from one carotid artery, the other being tied. They were then decerebrated through a trephine hole, and the vertebral arteries were compressed until bleeding from the transected mid-brain ceased.

Transections of the cord were done by removing the arch of the second cervical vertebra, incising the dura and passing under the spinal cord a thread, the tying of which completed the transection. In those experiments in which nerves were stimulated, the stimuli were either

induction shocks timed by the vibrating hammer, or, more usually, condenser discharges at a frequency controlled by a neon tube device. At the end of each experiment on the sympathectomized animals, a careful post-mortem examination showed that in all cats, with one exception, there were no remaining fragments of the sympathetic chain and that no regeneration had taken place. In the exceptional cat, short lengths of chain including three ganglia on one side and two on the other were found beneath the crura of the diaphragm. It is improbable that these fragments had any significant functional connexions, since the vascular reactions of this animal were in no way different from those in which the sympathectomy was demonstrably complete.

In connexion with experiments on the effects of stimulation of spinal nerve roots, we recorded the temperature of the hairless pads of the cat's hind foot. For this purpose we used an iron-constantan thermocouple of 36 gauge wire. The two wires were soldered together for 2 mm. and the junction so formed was fixed to the surface of the pad with adhesive cellophane tape. The cold junction was kept in ice in a vacuum flask, and the thermal currents were measured with a Moll galvanometer, a balancing current being applied to keep the galvanometer light on its scale. The sensitivity was such that changes of 0·1° C. could be detected with ease.

RESULTS

Effect of decerebration on blood pressure

In four of the sympathectomized cats, the blood pressure was recorded under ether before decerebration. The values observed varied between 80 and 120 mm. Hg from animal to animal. This, in our experience, is significantly lower than the blood pressure of normal cats similarly recorded. Decerebration has little effect on the resting blood-pressure level of the sympathectomized animal; any difference has been in the direction of increase. The pressures recorded after decerebration varied in different animals between 88 and 130 mm., values which are significantly lower than those found in normal cats after decerebration, in which the range has been 120–150 mm.

Vasomotor reflexes after decerebration

(*a*) *Effect of brief occlusion of the vertebral arteries.*

In the normal decerebrated cat occlusion of the vertebral arteries evokes a steep rise of blood pressure to a level some 80–100 % above its previous value. The heart rhythm is slowed during the first few seconds

of the rise and then accelerates. Removal of the clamp on the vertebral arteries is followed by a prompt return to the resting level, with occasionally a little overswing below (Fig. 1A). Removal of the suprarenals may reduce the extent of the rise of pressure, and accelerate the return of pressure to its normal level, but the general character of the effect is unaltered. After section of the vagi, the typical slowing of the heart is absent and the rise of blood pressure may be even more pronounced than in the cat with these nerves intact, and its return to its resting value less steep.

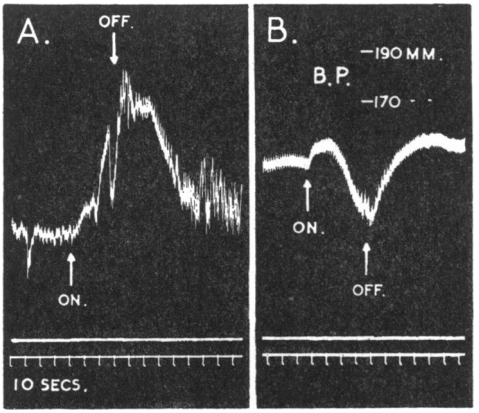

Fig. 1.

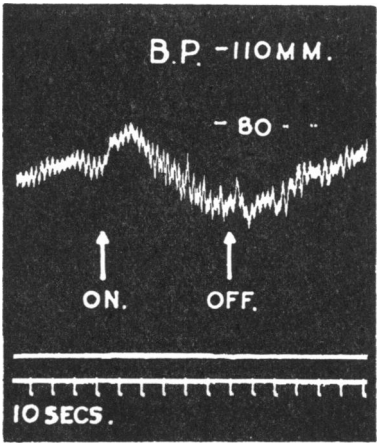

Fig. 2.

Fig. 1. Effect on blood pressure of occlusion of vertebral arteries. A, "normal" cat. B, cat, 2 weeks after sympathectomy.

Fig. 2. Effect on blood pressure of occlusion of vertebral arteries of cat 3 weeks after sympathectomy; both vagi cut.

The response of the sympathectomized cat to the same procedures is constantly the reverse of that described above. Tightening of the clamp causes a small and transient increase of blood pressure, but not more than can be accounted for by the further restriction thus caused of the blood flow to the head of the animal, and this quickly gives way to a fall, accompanied by a pronounced bradycardia (Fig. 1B). As might be expected, section of both vagi abolishes the slowing of the heart and reduces the degree of the depression of the blood pressure (Fig. 2). It is evident, however, that the fall of blood pressure is not entirely due to the vagal effect on the heart. In both the normal and the sympathectomized animal, vertebral clamping produces an extreme hyperpnoea and some muscular movements.

(*b*) *Effect of stimulation of sensory nerves.*

In the decerebrate normal cat, stimulation of the central end of the cut tibial or peroneal nerves produces widespread somatic reflex movements, with hyperpnoea, if the stimulus is of sufficient intensity, and a rise in blood pressure (Fig. 3A). In the sympathectomized cat, the somatic effects are identical, but the vascular response is always predominantly depressor (Figs. 3B, 7). The small initial pressor effect seen

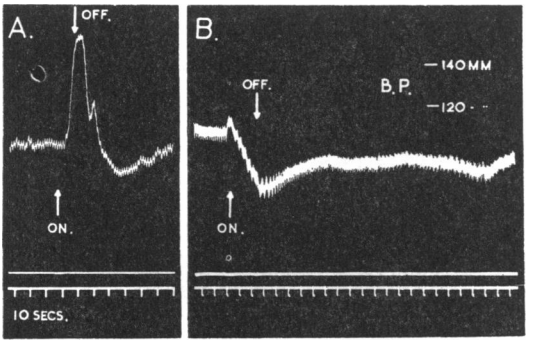

Fig. 3. Effect on blood pressure of stimulation of central end of cut tibial nerve. A, "normal" cat. B, cat, 2 weeks after sympathectomy.

in these figures we believe to be attributable to contraction of the abdominal muscles. Section of the vagi does not alter the depressor effect of sensory stimulation (Fig. 7A).

(*c*) *Effect of section of the spinal cord.*

As described under methods, the procedure for section of the spinal cord, which we have used, involves exposure of the cord at the level of the atlas, opening of the dura mater, the passage of a thread beneath the cord, and, finally, its section by tying the thread. Under the conditions of our experiments, in which the cord section was carried out on cats previously decerebrated and consequently freed from anaesthetic, the exposure, and, particularly, passage of the thread, was usually accompanied by considerable muscular movement.

Normal cats. In the normal cat, the preparation of the cord and its section evoked big rises of blood pressure, which were followed by a profound fall as the section became effective. That the rises of blood pressure, coincident with exposure and manipulation of the cord, are attributable to the excitation of efferent vasoconstrictor pathways in the cord is

made clear by the fact that they are absent when ether, in an amount sufficient to abolish decerebrate rigidity, is given after decerebration, and that they still are present when muscular movement is abolished by curarine (*vide infra*).

Sympathectomized cats. Entirely different effects follow exposure and section of the cord in the sympathectomized cat. In one experiment we were able to expose the cord and pass the ligature beneath it without

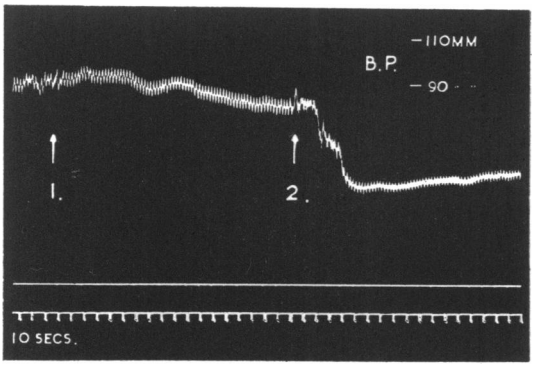

Fig. 4.

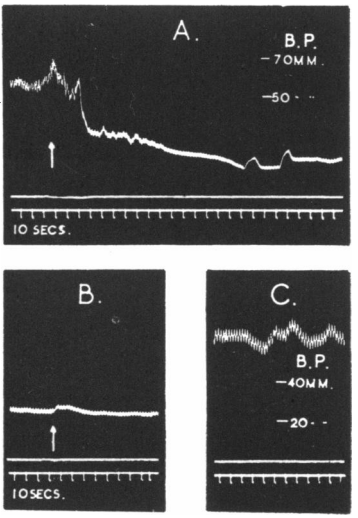

Fig. 5.

Fig. 4. Blood pressure of cat 2½ weeks after sympathectomy. At (1) thread passed under spinal cord; at (2) spinal cord transected.

Fig. 5. Blood pressure of cat 3 weeks after sympathectomy. A, effect of struggles produced by exposure of spinal cord. B, transection of cord 15 min. later. C, recovery of blood pressure 1 hr. later.

producing any irritation and consequent muscular movement. The blood pressure remained steady. Subsequent section of the cord produced an uncomplicated fall of blood pressure (Fig. 4). This experiment strongly suggested, at the time, that the section had inactivated some unknown pathway which had been maintaining vaso-motor tone. Our subsequent experiments have, however, shown that this deduction is not necessarily true. In all experiments, in which exposure of the cord caused muscular convulsions, a profound and lasting fall of blood pressure occurred, irrespective of whether the cord was cut or not (Fig. 5A). If the cord is cut at the depth of the fall of pressure, there is no further fall, and the

blood pressure gradually returns to the level at which it stood before the exposure of the cord (Fig. 5B, C). In one experiment in which exposure of the cord had produced a severe fall of pressure, the animal was allowed to rest, and some recovery of vascular tone took place. The cord was then frozen with CO_2 snow and cut while frozen. There were no muscular movements and no change in blood pressure. These experiments suggested that the main cause of the depressor responses in the sympathectomized cat might be the vaso-dilatation coincident with contraction of the voluntary muscles. We therefore investigated the responses to cord section, to clamping the vertebral arteries, and to sensory nerve stimulation in decerebrated normal and sympathectomized cats after administration of curarine.

Effect of curarine

(*a*) *Brief occlusion of vertebral arteries.* Full curarization of the normal decerebrated cat does not alter the vascular effects of brief occlusion of the vertebral arteries. (See p. 275.)

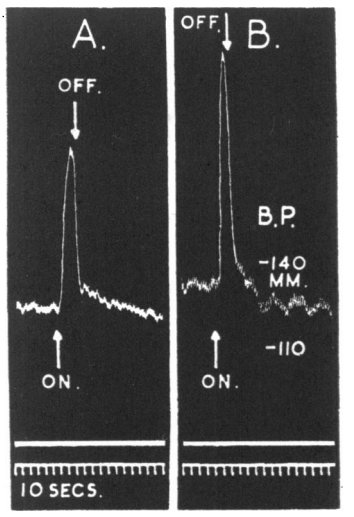

Fig. 6.

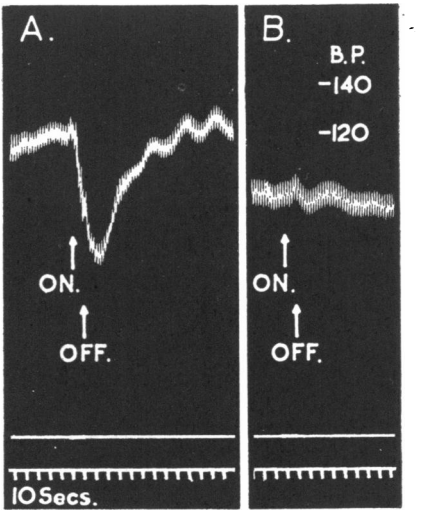

Fig. 7.

Fig. 6. Blood pressure of "normal" cat. Effect of stimulation of central end of cut tibial nerve. A, before; and B, after intravenous injection of 3 mg. of curarine.

Fig. 7. Effect on blood pressure of cat 3 weeks after sympathectomy, of stimulation of central end of cut tibial nerve, both vagi cut. A, before; and B, after intravenous injection of 3 mg. of curarine.

In the sympathectomized cat, the small fall of blood pressure, persisting in the response to vertebral clamping after bilateral vagotomy,

is no longer seen when the animal is curarized. Instead, there is a slight rise of blood pressure, so small indeed that it is impossible to attribute it with certainty to any cause other than the mere restriction of the circulation.

(*b*) *Sensory stimulation.* The production of complete neuromuscular block by curarine does not diminish the pressor responses of normal decerebrated cats to sensory nerve stimulation (Fig. 6). In the sympathectomized cat, the usual depressor effect of sensory stimulation is completely absent after curarine, and no change in blood pressure occurs (Fig. 7).

(*c*) *Cord section.* Section of the spinal cord of the decerebrated and *curarized* "normal" cat reproduced the characteristic rise and subsequent fall of blood pressure, which follow cord section in the cat without curare.

In the sympathectomized cat, on the other hand, curarine modifies profoundly the effect of cord section. In our earlier experiments we found that the usual depressor effects of irritation and section of the cord were absent after curarine[1], but in these animals the blood-pressure level at which cord section was performed was low (40–70 mm.), and this naturally suggested that any hypothetical vaso-constrictor mechanism was already out of action, and that section of the spinal cord could not, therefore, produce any further fall. This low blood pressure was usually the result of too rapid administration of curarine, which has by itself a vaso-dilator action, more conspicuous, perhaps, in sympathectomized animals. In two experiments, therefore, we took the precaution of administering the curarine in 0·25 mg. doses, spread over some 15 min., early in the experiment, removing the remaining suprarenal gland only when the animal was immobilized.

In one of these experiments, the blood pressure under curarine was 130 mm. Hg before the vertebrae were exposed. Removal of the bony arch of the second cervical vertebra was accompanied by a moderately sharp fall of blood pressure to 50 mm. Hg[1]. We then completed the exposure of the spinal cord and allowed the animal to rest for 20 min. The blood pressure gradually rose to 100 mm. Hg, and we then passed the thread under the cord and divided it. The blood pressure fell gradually to 70 mm. None of these procedures was accompanied by any muscular movements whatsoever. In the other experiment[1], the blood pressure was 90 mm. Hg after curarine had been given, but before exposure

[1] The three figures illustrating these points were lost after this paper had been received by the Editorial Board. The Board regrets this loss and the consequent delay in the publication of this paper.

of the cord. The neural arch of the vertebra was removed and the dura incised without any immediate change in blood pressure; then the blood pressure suddenly declined to 50 mm. without any new procedure or any other explanation for such a fall. After a rest of 20 min., the blood pressure had recovered to 70 mm., and section of the spinal cord then produced no change.

These experiments suggested the existence of some delicate vasomotor mechanism, in part responsible for vascular tone and dependent on the maintained functional connexion of the spinal cord with the medullary centres. The spontaneous recovery and maintenance of the blood pressure after cord section (cf. Fig. 5) shows, however, that this is not the sole factor involved. In any case, the relatively crude experiment of section of the spinal cord was obviously not suitable for demonstration of such a system, and we therefore attempted to modify medullary activity by other means.

Effect of prolonged occlusion of the vertebral arteries

Normal cats. The cats were decerebrated, fully curarized and under artificial respiration. We have already noted the immediate effects of clamping the vertebral arteries. If the clamp is left in position for some 15 min., the blood pressure gradually declines from its high level, but remains not much below its height before clamping. During this period, stimulation of the central end of one vagus is ineffective, i.e. one must regard the medulla as being at least partially paralysed by the ischaemia. When the clamp is loosened, the blood pressure returns to its normal level, and the depressor reflex can again be elicited. A renewed application of the clamp, however, evokes, not a sudden rise of blood pressure as it does on the first application, but an abrupt and permanent fall. Stimulation of the central end of the vagus is then permanently without effect. It is obvious that the second clamping has caused a lasting paralysis of the medullary centres.

Sympathectomized cats. The conditions were the same as for the normal cats. The first application of the vertebral clamp (for 15 min.) had no lasting effect on the blood pressure, apart from the small initial rise, which we have already described. The second clamping produced, after a latency of 7 min., a gradual, but profound and permanent fall of blood pressure. In these experiments both vagus nerves had been previously cut in the neck.

Effects of stimulation of anterior roots

The almost complete abolition by curarine of vaso-motor response in the sympathectomized cats had naturally suggested that the depressor effects of sensory stimulation and similar procedures were caused by muscular movements and the consequent vaso-dilatation in the muscles. We have, therefore, recorded the effects on the general blood pressure of stimulation of the anterior lumbar spinal roots in normal and in sympathectomized cats.

Normal cats. In the normal cat, the immediate effect of stimulation of the anterior roots at a tetanizing frequency (50 per sec.) is a rise of blood pressure. As the stimulation is continued, the blood pressure

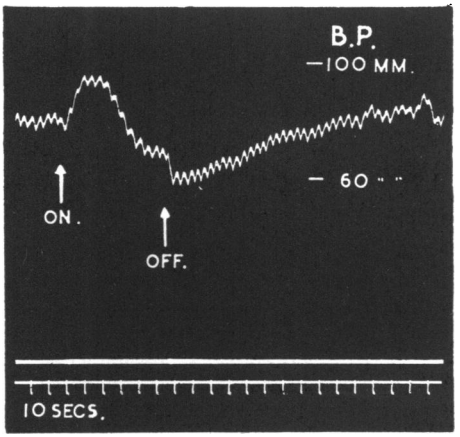

Fig. 8. Effect on blood pressure of "normal" cat of stimulation of anterior spinal roots (sixth and seventh post-thoracic).

returns towards normal, and, at the end of a stimulation lasting a minute, it may even be lower than the resting level. Cessation of the stimulation is, in any case, accompanied by an abrupt, though not large, further fall in pressure and a gradual recovery (Fig. 8). The recovery of blood pressure is complete in from 2 to 3 min. With a stimulation of shorter duration, the entire effect during stimulation is pressor, but the sudden drop of pressure on stopping the stimulus is still in evidence, and is quickly followed by a compensatory rebound, which carries the blood pressure to a level as high as it attained during the stimulation.

Sympathectomized cats. Stimulation of the anterior roots in the sympathectomized cat produces an initial rise in blood pressure of a few

seconds' duration, succeeded by a steep fall, which continues after the cessation of stimulation. A recovery follows, but it is so gradual that the initial level of blood pressure is not attained until after 10–15 min. (Fig. 9A). The administration of curarine, in a dose sufficient completely to abolish the visible response of the muscles to motor nerve stimulation, entirely prevents the fall of blood pressure evoked by excitation of the

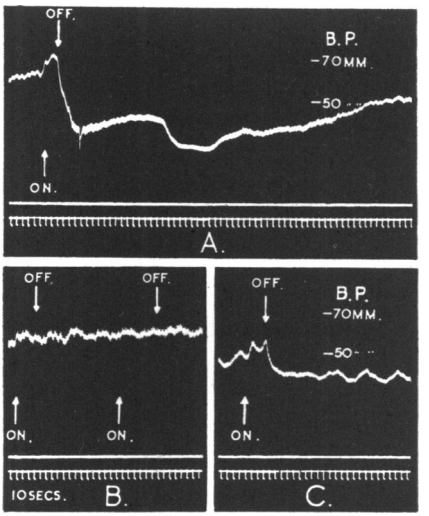

Fig. 9. Blood pressure of cat 2 weeks after sympathectomy. A, stimulation of anterior spinal roots (sixth and seventh post-thoracic). B, stimulation of anterior roots after 2 mg. curarine. C, direct stimulation of leg muscles 32 min. later.

anterior roots (Fig. 9B). Under these conditions, however, the production of muscular movements by direct stimulation of the limb muscles, through electrodes buried in them, is still accompanied by a fall of blood pressure (Fig. 9C).

Stimulation of dorsal roots

Rosenblueth & Cannon [1934] suggested that the abolition of depressor vascular reflexes in the sympathectomized cat by curare was due to the paralysing effect of curare upon dorsal root dilator fibres. In a later paper from the same laboratory, Pinkston *et al.* [1936] state that curare abolishes vaso-motor reflexes in sympathectomized cats, and this is taken as evidence that "the vaso-dilator fibres in question are the dorsal root dilators". As evidence that curare abolishes the effects of dorsal root stimulation, Rosenblueth & Cannon [1934] refer to Bayliss [1923]. We

have been unable to discover any reference by Bayliss [1923] to such an action of curare; on the contrary, Bayliss [1900] makes it quite clear that the effects of antidromic excitation can be obtained in fully curarized animals, provided the initial vaso-dilatation normally produced by curare is allowed to pass off. (See also Langley, 1923.)

We ourselves have been able to demonstrate that antidromic vaso-dilatation persists in the cat paralysed with curarine. Changes in the cutaneous temperature of the pad of the hind paw of the cat were used as an index of the state of the tone of the vessels, in the manner described by Wybauw [1936]. The greatest rises in pad temperature were obtained by stimulation of the seventh post-thoracic dorsal root (Fig. 10). The administration of the first dose of 1 mg. of curarine caused a rise in pad temperature of 2·5° C.—a rise considerably greater than any we have ever produced by stimulation. This dose was sufficient to block neuro-muscular conduction, but stimulation of the posterior roots still produced a rise in temperature of 0·9° C., quite definite, though somewhat less than that observed in the same experiment before curarine (1·4° C.). A second dose of 1 mg. of curarine produced a rise of temperature of about 1° C. and, when the temperature had again fallen, stimulation still evoked a rise of 0·7° C. (Fig. 10). In any case, apart from the diminished response of vessels already partially diluted by curarine, a diminution in the effectiveness of successive stimulations is to be expected, for Wybauw has reported, and we ourselves have observed, that the response in the cat without curarine progressively decreases and finally disappears.

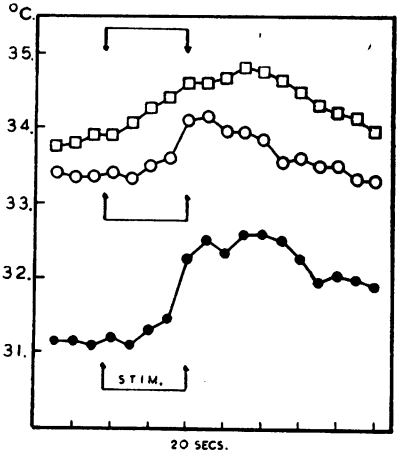

Fig. 10. Effect of stimulation of posterior roots on pad temperature. • Before curarine; □ after 1 mg. curarine; o after a further 1 mg. curarine.

Discussion

The primary object of these experiments on animals deprived of their sympathetic chains has been to determine the means whereby such animals regulate and maintain their vascular tone. Ample evidence is available from previous investigations to show that the sympathectomized animal has a resting blood pressure little different from the normal, and

there is no doubt that blood vessels, whether normal, or deprived by degeneration of their sympathetic innervation, can develop and maintain a spontaneous tone. The vessels of the extremities perfused with blood [Burn & Dale, 1926], or haemoglobin solution [Brown & Dale, 1936], react normally to vaso-dilator substances like histamine and acetylcholine, and our own experience shows that this applies to the reactions of the perfused hind limbs of the completely sympathectomized cat, in which the tone of the vessels recovers with normal promptitude from the dilator effect of a small dose of histamine or acetylcholine. Indeed, the depressor effects of these substances retain their normal evanescence in the intact circulation of the sympathectomized cat.

As our aim in this investigation was a study of the vaso-motor activity of the central nervous system, we have tried to use preparations in which that activity was as little depressed as possible, and for that reason we have used decerebrate animals, both for our control experiments, and for the final experiment on the cat after the sympathectomy has been completed.

Bacq *et al.* [1934] have claimed that occlusion of the carotid arteries in the totally sympathectomized cat causes a reflex arterial hypertension of 40–50 mm. Hg. Pinkston *et al.* [1936] and Thomas & Brooks [1935, 1937] have been unable to obtain similar results, but Bacq, Bremer, Brouha & Heymans [1937, 1939] have repeated their original experiments with some modifications of technique, and have been able to confirm the original findings of Bacq *et al.* [1934]. We have not attempted to repeat the experiments of Bacq *et al.* [1934]; indeed, the ligation of the carotid arteries, which we have always carried out as a preliminary to decerebration, has precluded any investigation of carotid sinus reflexes. Under these conditions, we have never observed a genuine pressor response of any sort to any form of stimulation. We have admittedly recorded many small rises of blood pressure of a few mm. in extent and lasting a few seconds (Figs. 3, 9), but in all instances these have been immediately coincident with the onset of somatic muscular movements, e.g. of limbs, of the abdominal wall, or of the respiratory musculature. We are inclined to ascribe these small and evanescent pressor changes to the mechanical disturbances so produced in the vascular bed, and to credit them with no significance as indications of vaso-constriction.

Undoubtedly, in the absence of the carotid sinuses the most predominant vascular response of the sympathectomized cat to any stimulus is a fall of blood pressure. Brief occlusion of the vertebral arteries and sensory nerve stimulation both cause a fall of blood pressure, and this fall is, in both instances, abolished by curarization of the animal.

Stimulation of the anterior spinal roots in the sympathectomized animal produces a similar fall of blood pressure, and this again is abolished by curarization. These observations strongly suggest that the depressor responses, which are so common in the sympathectomized cats, are all attributable to the vaso-dilatation accompanying and consequent on muscular movement. In this assumption we are, in the main, in agreement with Bacq *et al.* [1934], in that they attribute the fall of blood pressure produced by struggling to the peripheral action of muscular metabolites. Rosenblueth & Cannon [1934], Freeman & Rosenblueth [1932] and Pinkston *et al.* [1936], on the other hand, do not believe that muscular metabolites play more than a minor part in the production of such falls of blood pressure. They postulate the existence of a vaso-dilator system with a centre in the medulla and a peripheral pathway *via* the posterior roots, changes in the "tone" of which mediate dilator and constrictor reflexes in sympathectomized cats. We ourselves have been unable to obtain any evidence of the existence of such a mechanism. The conception of the existence of these fibres is based by Pinkston *et al.* [1936] on the abolition of the vaso-dilator reaction by curare and the presence of "depressor points" in the floor of the fourth ventricle. As we have shown experimentally, antidromic vaso-dilatation can occur readily in the cat under curarine, and in any case it is difficult to conceive of any point in the posterior root pathway at which curarine could act. Curarine, suitably applied, has a paralysing effect upon sympathetic ganglion cells [Brown & Feldberg, 1936], but the posterior root ganglion cells are not synaptic and are entirely resistant to the action of nicotine, even when they lie directly in the path of the nerve impulse, as in the skate [Langley, 1901]. Any action of curarine in abolishing vaso-dilator activity could only, if Pinkston *et al.* [1936] were correct, be attributed to a central action. The only evidence that curarine has such a central action is the finding of Rosenblueth & Cannon [1934] that "curare causes a rise of blood pressure in sympathectomized cats". Purified curarine chloride, on the other hand, has, in our experience, always produced a fall of blood pressure in both normal and sympathectomized cats, unless it is administered very slowly, when the blood pressure is unaffected. Similarly, spinal anaesthesia and spinal transection might be expected to cause a rise of blood pressure through the interruption of the vaso-dilator pathways. Bacq *et al.* [1934] and Bradshaw [1936] record respectively a fall of pressure and no effect following spinal anaesthesia, and all authors agree that spinal transection, in the absence of curare, causes a fall of blood pressure.

It is in the interpretation of the effects of spinal transection that we have encountered most difficulty. Most of our evidence points clearly to the fact that the profound and sudden fall of blood pressure, which results from irritation or section of the spinal cord in the sympathectomized cat, is attributable largely to the vaso-dilatation consequent on muscular movement. Nevertheless, exposure of the spinal cord, its section, or ischaemia of the medullary centres, may cause a fall of blood pressure in the sympathectomized cat, even after section of the vagi and full curarization. It might be suggested that such a fall of blood pressure, persisting after full curarization, might still be attributable to motor-nerve impulses, which have been shown to liberate acetylcholine at the motor-nerve endings, even in full curarization [Dale, Feldberg & Vogt, 1936]. These authors have shown that this acetylcholine may diffuse sufficiently to have a local vaso-dilator action, but only in the presence of eserine. In any case, in our own experiments the very considerable falls of blood pressure evoked by direct anterior-root stimulation were completely eliminated by curarization. This seems effectively to exclude not only acetylcholine, but any other vaso-dilator substance, if such were liberated by motor-nerve impulses in the absence of muscular contractions from participation in these falls of blood pressure. We can see no alternative to the conclusion that this fall of blood pressure, following exposure or section of the cord under curarine, is due to the interruption or disorganization of a central vaso-constrictor tone, the effect of which is conveyed to the periphery by some extra-sympathetic path.

Whatever this may be, it is a delicate and sensitive mechanism, which is in action only when the blood pressure is in the region of 100 mm. Hg. In postulating such an unknown pathway, we are in agreement with Bacq *et al.* [1934], who invoked the existence of such a system to explain the occurrence of carotid sinus reflexes, and who believe that its presence can only be demonstrated when the resting blood pressure is at least 100 mm. Hg. We are further investigating its nature.

Whatever may be the functional significance of such a pathway, our experiments have at least shown that its vaso-constrictor activities are readily overpowered by the vaso-dilatation produced by muscular movement, and that this latter factor must be rigidly controlled in any experiments on sympathectomized cats. Indeed, it is the lability of their blood pressure, when they are in any state other than full curarization, which complicates any investigation of the control of the vascular tone of these animals.

SUMMARY

1. The vascular reactions of the cat have been investigated after extirpation of the sympathetic chains.

2. Stimulation of sensory nerves and of anterior spinal roots, brief occlusion of the vertebral arteries and irritation or transection of the spinal cord, produce falls of blood pressure.

3. Abolition of the coincident muscular movements by curarine prevents the occurrence of these falls of blood pressure wholly, in the instance of sensory nerve, or anterior root stimulation, and brief vertebral occlusion.

4. Curarine also abolishes the depressor effect of spinal irritation or transection when the blood pressure is low.

5. If the blood pressure is high, manipulation or transection of the spinal cord causes a fall of blood pressure, even if the cat is immobilized completely by curarine. This suggests the existence of a vaso-constrictor pathway other than the thoracico-lumbar outflow.

6. The predominant factor in the vascular reactions of the sympathectomized cat is, nevertheless, the vaso-dilatation accompanying contraction of the skeletal muscles.

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