VASO-MOTOR CENTRES. Part III. Spinal vascular (and other autonomic) reflexes and the effect of strychnine on them.

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CONTENTS.

THE aim of the experiments given in this paper was to see if any explanation could be given of the varying results which previous observers have obtained in animals a short time after section of the spinal cord, by stimulating the central end of a sensory nerve both before and after injecting strychnine.

In what follows, I speak, for the sake of brevity, of "stimulating a nerve" instead of "stimulating the central end of a nerve." In all cases the nerve was tied and cut.

Method. The experiments were made on cats. The cats were anæsthetised with chloroform, tracheotomy performed and anæsthesia continued with C.E. mixture till the animal was decerebrated or decapitated. The decerebration was in nearly all cases by the guillotine. Both vagi were cut, the necessary cannulæ inserted, the nerves to be stimulated tied and cut, the spinal cord exposed in the region to be transected. This region was usually the mid-cervical, in two experiments the 8th cervical to 2nd thoracic. A carotid blood-pressure tracing was taken, the spinal cord cut, curari injected in just sufficient quantity to paralyse the somatic motor nerves, the nerves stimulated two or more times. In most cases strychnine was injected in successive doses, and the nerves stimulated two or more times after each injection. This method was used in order to meet the possible objection that in decapitation the

vaso-motor centre is not wholly severed from the spinal cord. By it some idea of the excitability of the spinal centres is gathered from the extent of the rise of blood-pressure produced by the section of the spinal cord. Decapitation[1] was performed after ligature of the arteries by Sherrington's method. In a few experiments, after decapitation, the cord was again cut in the mid-cervical region. Sometimes instead of cutting off the head after section of the cord, the brain was destroyed.

No certain difference was found in the results of nerve stimulation with these and other minor variations of method, *i.e.* the presence of the upper cervical portion of the spinal cord did not appreciably affect the results. The blood-pressure in the individual spinal animals, for the first half hour or more, varied considerably; it was usually 60–70 mm. Hg, sometimes only 40–50 mm., but occasionally more than 100 mm. Hg. The variation was found whichever method of obtaining a spinal animal was employed, but on the average the pressure was lower when the animal was decerebrated, and the cervical cord cut, probably in consequence of the greater loss of blood and the longer duration of dissection. A high blood-pressure probably means stimulation of the cut surface of the cord, either by blood clots or by swabs sometimes used to check oozing from the anterior spinal artery. Ustimovitch(1) found in the dog that after section of the cord, the blood-pressure slowly sank. According to Sherrington(2) the pressure in the cat after decapitation is 70–90 mm., and is higher an hour or so after the decapitation than earlier. In my experiments, in which nerve stimulation was begun soon after cord section, the blood-pressure invariably sank, except for temporary rises when strychnine was injected. The pressure is somewhat greater when the preparation is on its side than on its back owing to slight compression of the liver and other viscera.

Stimulation was by the interrupted current of an induction coil, the current being, as a rule, fairly strongly felt on the tongue. Since it has been shown that the reflex rise of blood-pressure caused by the nerves of the limbs in spinal animals, if it occurs at all, is at most small, the nerve to be stimulated must either be arranged so that it can be stimulated without any movement or pressure on the body, or (preferably) the nerve must be placed on electrodes held in a stand. A large nerve such as the sciatic should be laid between the electrode terminals and not simply laid on them. Further it is not safe to infer an absence of reflex from the sciatic until a very strong current has been used.

[1] After cutting the spinal cord the occipito-atlantoid joint is I think more easily found if the tissues at the side of the neck are first cut up to the vertebræ

A difficulty which not infrequently occurs in the way of determining whether there is or is not a small rise of blood-pressure is that for some time after the cord is cut, there are 3rd order waves[1] in the blood-pressure tracing. These vary greatly in size in different experiments. Usually they are only 2–3 mm. in height but in one experiment waves of 16 to 20 mm. continued for about a quarter of an hour. Whilst they usually occur at fairly regular intervals, they do not always do so, and whether there is a slight reflex effect can only be told by an examination of the whole of the tracing. A *complete* disappearance of variations in the tracing may mean that the excitability of the spinal cord is very small. It is advisable to test the excitability at the end of an experiment by noting what rise of blood-pressure and erection of hairs is caused by asphyxia.

Observations on un-curarised spinal animals are untrustworthy, since contraction of abdominal muscles or of the diaphragm readily causes a slight rise of blood-pressure. Contraction confined to a leg may do so, but often does not. It must be borne in mind that curari paralyses the muscles of the diaphragm later than those of the limbs and trunk.

Spinal Vascular Reflexes from Limb and Trunk Nerves.

Reflexes on carotid[2] blood-pressure.

Limb nerves. In the early experiments in Ludwig's laboratory, no rise of general blood-pressure was obtained in rabbits by stimulating the sciatic after section of the spinal cord just below the spinal bulb. An absence of result has also been obtained by several subsequent observers, but some have found that a rise or fall of carotid blood-pressure of a few millimetres of mercury was at times, though not constantly, obtained. In rabbits and cats an effect, when obtained, was a rise of blood-pressure, in dogs it was usually a fall.

Owsjannikoff(3) obtained in the rabbit no rise of blood-pressure from the sciatic, S. Mayer(4) found none in the dog, Dittmar(5) confirmed Owsjannikoff's result in the rabbit. Schlesinger(6) obtained none from the median nerve. Bochefontaine(7) tied the spinal cord of the dog above the axis and found that the sciatic caused a rise of blood-pressure of 20–25 mm. Hg. Whether this was a spinal reflex is doubtful since after the ligature, section of the dura mater of the brain caused slowing of the heart and a still greater rise of blood-pressure. Kabierski and Heidenhain(8) in experiments on rabbits in which the carotid and vertebral arteries were tied obtained a rise of blood-pressure from the sciatic in 7 out of 20 experiments, the rise varying from 1–10 mm. Hg. When the spinal cord was cut, a rise was more rarely obtained. Dogs were said to be less, and cats

[1] I include in these all waves which cannot be considered as synchronous with variations in the size of the thorax.

[2] The blood-pressure as taken in the carotid is of course the aortic blood-pressure.

more favourable for obtaining a trifling rise. Luchsinger(9) seldom found a rise from the sciatic in cats and rabbits and when it occurred it was trifling. Stricker(10) sometimes obtained a rise up to 50 mm. Hg from the sciatic in dogs, but as curari was not given it is uncertain how far the rise was due to muscular contraction and movement, and apparently he found no rise after curari had been injected. Smirnoff(11) found that when the spinal cord was cut in the dog just above the 1st thoracic vertebra the brachial nerves had no effect, and the sciatic caused either none, or a slight rise with the first stimulus only; that when the cord was cut below the 6th vertebra the sciatic nerve had no effect and the brachial nerves also had none, or caused a slight fall with the first stimulus only, but that after section between the 1st and 6th thoracic vertebræ, the brachial nerves caused a fall of blood-pressure and the sciatic caused a rise. The negative results in these experiments are undoubtedly untrustworthy. Ustimovitch(1) usually obtained from the sciatic of the rabbit a rise of 2 to 4 mm., the maximum being 8 mm.; in the dog the sciatic frequently caused a fall of blood-pressure and very seldom a rise. Muscular movement was not prevented by curari. Thayer and Pal(12) found that both the sciatic and brachial nerves in the dog caused a fall of blood-pressure and caused it after section of the splanchnic and of the limb nerves; the sciatic still caused a fall after section of the cord in the thoracic or lumbar region. Asher and Lüscher(13) obtained a very small reflex rise from the sciatic in rabbits made spinal by injecting paraffin into the carotid arteries and un-curarised. Jappelli(14) stimulated the sciatic in the dog with a series of brief tetanic currents during cessation of artificial respiration. In curarised animals, he found no effect at first but somewhat later and before any marked asphyctic rise of blood-pressure, he obtained a series of rather irregular slight rises which tended to be synchronous with the stimuli. When curari was not given, a slight rise was caused by each of a series of single induction shocks. Pike(15) obtained no effect from the sciatic of the cat after giving curari. Sherrington ((16), p. 143) very rarely obtained in cats any vaso-motor reflex from the sciatic and/or other somatic nerve.

The sciatic or one of its branches—usually the musculo-cutaneous (superficial peroneal) was stimulated after section of the spinal cord and injection of curari in 18 experiments besides those to be mentioned later in which the abdominal viscera were exposed or excised. In 15 of these experiments the nerve was stimulated (1 to 5 times) in the first half hour after cord section and strychnine was then injected. In the last three (cp. p. 238) the stimulations were for a longer period before strychnine was injected.

In nine experiments there was a definite though trifling rise of blood-pressure. The rise varied with the successive stimulations usually from 1½ to 5 mm. and in one experiment from 1½ to 7 mm. When shallow 3rd order waves were already present the stimulation increased the height of one or two of them. When the curve ran an even course, stimulation usually caused two waves of rise of pressure and sometimes more. Fig. 1 gives two typical examples of the effect of sciatic stimulation.

In six experiments there was a rise of pressure of 1 to 2 mm. with one or two of the stimulations, but in an equal or greater number of stimulations there was no effect.

In three experiments, stimulation had no effect, in two of these, however, the nerve was stimulated once only before giving strychnine

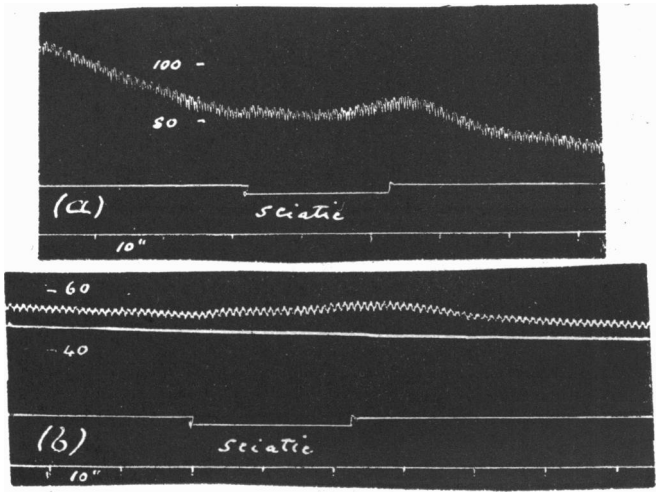

Fig. 1. Cats, decerebrated, vagi cut, curarised. (*a*) Spinal cord cut between 3rd and 4th cervical segment. Stimulation of sciatic near the end of the rise of blood-pressure caused by the section. (*b*) From another experiment. Cord cut between 1st and 2nd thoracic. Stimulation when the blood-pressure had fallen to a nearly constant level.

(cp. Exp. 1, p. 243). There were two other experiments in which the sciatic had no effect, but in these the carotid pressure was only 30–25 mm. Hg and section of the cord caused a small rise only, showing that the excitability of the cord had greatly decreased.

In eight experiments, one or more of the brachial nerves was stimulated. The results were much as those with the sciatic but on the whole the rise was less (though once it was 7 mm.) and was less frequently obtained.

In connexion with observations on the degree of restriction in the viscera of the vascular reflexes (p. 240) four experiments were made in which the spinal animal was placed in Ringer's fluid at 38–39° C., the abdominal viscera exposed and the fore and hind leg nerves stimulated. In each of these a slight rise of blood-pressure was obtained. The rise from the median, ulnar and superficial peroneal was 2–4 mm. The sciatic was stimulated in one experiment only, it caused a rise of 7–8 mm. and it set up a series of 3rd order waves (Fig. 2).

Lower thoracic and upper lumbar cutaneous nerves. It seemed possible

that the lower thoracic and lumbar nerves, since they arise from the region of the spinal cord containing the vaso-constrictor nerve cells,

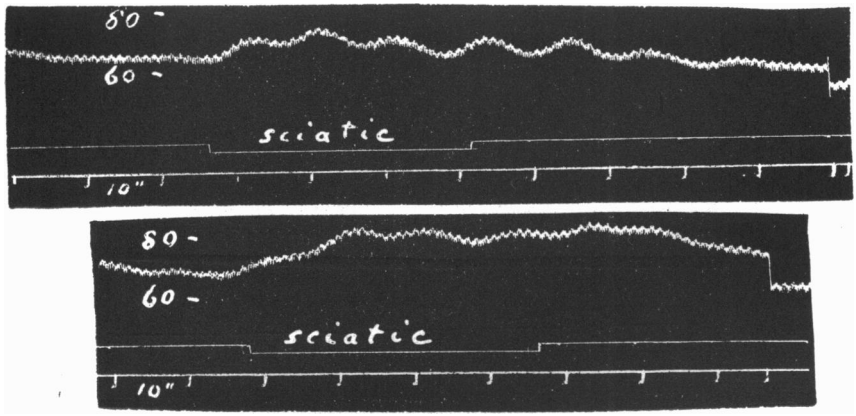

Fig. 2. Spinal cat (1st cerv.; brain destroyed, curarised) in warm Ringer's fluid, abdominal viscera exposed. Two stimulations of the sciatic.

might have a greater effect than the sciatic. Nine experiments were made in which the cutaneous branches of one or more of the 13 thoracic to 2nd lumbar nerves were cut and the central ends stimulated. In two experiments there was no effect, in one it was doubtful whether there was an effect or not, in two there was a trace of rise of blood-pressure, in two the rise varied from $\frac{1}{2}$ to 2 mm. Hg; and in two the rise varied from 2–7 mm. Hg. The results then were much the same as those obtained with the limb nerves, though the number of nerve fibres stimulated was less.

The foregoing experiments show that a trifling rise of general arterial blood-pressure can usually be obtained from the limb and trunk nerves of the spinal cat. The fact suggests that an absence of reflex rise must be due to some experimental condition. A considerable loss of blood, a low blood-pressure, a longer duration of low blood-pressure are unfavourable for the production of a reflex rise, but not a few of the variations in the results could not satsifactorily be explained by variations in these conditions. Loss of blood in somewhat greater quantity than usual seemed to make the results inconstant, but increasing its volume—and the blood-pressure—by injecting gum saline did not make the results more constant. Raising the blood-pressure by adrenaline, or by stimulation of the spinal cord had also no constant effect on the

reflexes. Low blood-pressure, if not too prolonged, did not necessarily abolish the reflex; thus in one experiment the blood-pressure fell to 27–24 mm. Hg, yet the sciatic caused a rise of 1½ mm. in each of three stimulations in the subsequent quarter of an hour. In this experiment the mid-cervical region of the spinal cord was frozen with liquid air before being cut; since its section caused no rise of blood-pressure, the occurrence of a reflex rise might be attributed to an absence of fatigue, but sometimes the sciatic will cause a rise of blood-pressure almost immediately after a very large rise has been caused by stimulation of the cord either mechanically by section (cp. Fig. 1, *a*) or by electrical stimulation. Moreover such variations in condition do not account for the variable effect of successive stimulations, in any one experiment. For whilst the effect depends to some extent on the interval between the stimulations, the effect may also be variable when the interval is two to three minutes. Section of the cord no doubt produces different degrees of "shock," *i.e.* of depression of activity of the spinal centres in different cats, but judging the excitability by the response to electrical stimulation, strychnine and asphyxia, the spinal vaso-motor centres may be very excitable and yet fail to give a reflex to one or more stimulations of a limb or trunk nerve.

These considerations suggested that one of the factors causing variation in the reflex rise, in addition to those mentioned, is a difference in the response of the peripheral vessels. If such existed, it seemed probable that it would be in the vessels of the abdominal viscera, and as a first step in the investigation of this, the effect of removing the abdominal viscera was tried.

Reflex on carotid pressure after evisceration. In four experiments, the intestine, stomach, pancreas, and spleen were excised, and in one of these the left kidney and adrenal gland also. If, in doing this, the intestine is exposed, it contracts, nearly empties its blood vessels, and the blood-pressure is for a time increased; in one case, the carotid pressure, even after injecting curari was 118 mm. Hg. In one or other of the experiments, the posterior tibial, the superficial peroneal, the sciatic, and the median nerve were stimulated. Most stimuli had either no effect or a doubtful one. With none was there a rise of more than 2 mm. Hg. The experiments indicated that the reflex rise ordinarily obtained is chiefly due to contraction of the vessels of the viscera, but that the contraction is not confined to these.

Effect of digestion. In 15 of the 18 experiments mentioned above, the animal was fed the evening before being anæsthetised and the remains

of the meal may have been eaten in the morning, *i.e.* the animals may have been in different digestive states. In order to determine whether the state of digestion influenced the reflex rise, the last three experiments were made on cats fed with milk, or milk and meat, two hours before being anæsthetised. In each, a slight rise of blood-pressure was obtained by stimulating the sciatic. In two of the experiments a closely similar rise was obtained with each of more than half a dozen stimulations; one of these is shown in Fig. 3. In the third experiment the rise was variable and inconstant. But I think it may be concluded that one of the chief factors determining the variability in the occurrence of a reflex rise of blood-pressure is the state of digestion. As will be described later, digestion has a great influence on the reflex rise of pressure after strychnine

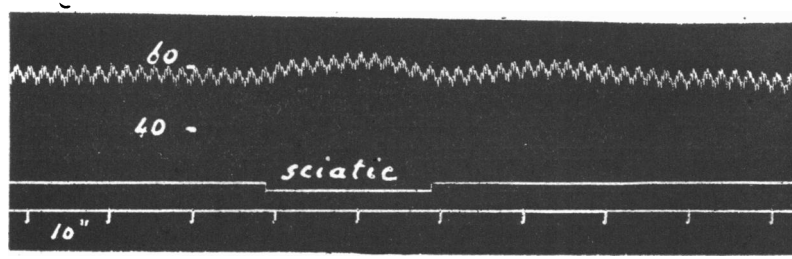

Fig. 3. Cat in full digestion. Cord cut at 1st cervical segment, brain destroyed, curarised. The figure shows one of a series of eight sciatic stimulations, each giving the same effect.

has been injected. The more constant effect in digestion is probably due to an increase in the volume of the blood, though, as I have said, I have not found that injecting gum saline has any certain effect in increasing the reflex rise of blood-pressure or in making it more constant.

In view of the results in the digesting spinal animal and of the frequency with which a trifling rise of blood-pressure is obtained in hungry or slightly digesting spinal animals, I conclude that when afferent nerve stimulation causes no rise of blood-pressure it is in consequence of one or more of the experimental conditions which tend to prevent it, notwithstanding that in some cases the conditions concerned are not definitely ascertainable.

Local reflexes and reflexes other than vaso-constrictor.

The small rise of general arterial pressure caused by the limb nerves in "acute" experiments on spinal cats can hardly be regarded as of any

importance in modifying the circulation in normal conditions. So far there is little reason to doubt the theory that spinal vaso-constrictor reflexes are normally unimportant[1]. But this is only true if the reflex vaso-constriction is widespread. At a certain degree of limitation of the area of vaso-constriction, the reflex would become important, for the smaller the area, the more completely the blood must be cut off from it in order to cause a rise of a few millimetres of general arterial pressure.

That the spinal cord serves the purpose of producing local constriction of blood vessels has been suggested by Vulpian(17) and by Kabierski and Heidenhain(8) and by some later observers. Neither the experiments of Vulpian nor of Kabierski and Heidenhain are satisfactory on this point. Vulpian on stimulating the sciatic (dog) on one side after section of the spinal cord found a fall of temperature in the foot of the opposite side. How much of the rest of the body was affected was not determined. The local action was presumably deduced from his observation that stimulation of the toes or web caused a rise of temperature in the foot on the same side. No evidence, however, was given that the effect was produced reflexly, for local dilatation is readily produced by direct stimulation. Kabierski and Heidenhain stated that no reflex rise of blood-pressure was produced from the sciatic after section of the cord in the lower thoracic region and argued that this was a consequence of the vaso-constrictor effect from the upper part of the cord being cut off so that the area affected was too restricted to cause a rise. The statement is inconsistent with their suggestion of local action. At this date the extended area innervated by the sympathetic fibres of each spinal nerve was imperfectly appreciated. With our present knowledge it is practically certain that no spinal sympathetic reflex can be confined to the area of a single spinal nerve. Except in cases of exaggerated local excitability the minimal area is probably that of three nerves. To determine the area affected in the skin would require numerous experiments by the thermo-electric method, but ocular inspection affords a simple means of determining whether any considerable local vaso-constriction occurs.

Comparative observations were made on the colour of the fore and hind feet and on the colour and contraction of the viscera in cats after decapitation or destruction of the brain.

Colour of feet. In different experiments, the posterior tibial nerve, the

[1] This argument would of course not hold if it could be shown that section of the cord decreases the excitability of a part of the reflex arc with which the descending spinal nerve fibres are not connected.

superficial peroneal nerve on one or both sides and the sciatic were stimulated. In the fore feet no certain change of colour was seen. In the hind feet there was sometimes, but not constantly, slight paling of both hind feet, or slight flushing, or slight paling preceded by flushing; the flushing was more frequently on the side opposite to that stimulated. Thus there was evidence of a trifling vascular reflex, both vaso-constrictor and vaso-dilator, not extending to the fore feet, but it was clear that no marked vaso-constrictor or vaso-dilator reflex occurred. The blood-pressure in these experiments was 50–65 mm. Hg; the flushing would no doubt have been greater with a normal blood-pressure.

Change of colour and other effects on the viscera. In four experiments, after section of the spinal cord at the 1st cervical segment, decapitation or destruction of the brain and curarisation, the spinal animal was placed in Ringer's fluid at 38–39° C. and the abdominal viscera exposed. The superficial peroneal nerve and one or more of the nerves of the fore limb above the elbow were stimulated. The effect of successive stimulations was not constant, but sometimes the hind limb nerve caused distinct pallor of the proximal colon, and apparently some of the lower part of the ileum, whilst the fore limb nerves caused pallor of the duodenum and apparently of the stomach. After several stimulations the middle part of the intestine was markedly less pale than the rest.

Incidental observations were made on other reflexes. The hind limb nerves caused slight but distinct contraction of the bladder and this was not seen on stimulating the fore limb nerves. It may be recalled that Schlesinger(6) in spinal rabbits obtained contraction of the uterus on stimulating the sciatic nerve, sometimes by stimulating the anterior crural but not by stimulating the brachial nerves.

In each experiment anti-peristaltic (anastaltic) waves occurred in the proximal colon. Stimulation of the superficial peroneal nerve appeared to increase these, and occasionally to stop them; occasionally, too, its stimulation was followed by inhibition of the rhythmic movement of the ileum, suggesting a fairly general slight action on the autonomic centres of the lower part of the spinal cord.

The results show I think some degree of local reflex action from the limb nerves, but they do not show any great restriction of effect. I had hoped that the degree of local action could be definitely determined by observing the areas in which erection of the hairs occurred. Unfortunately for this aim, stimulation of afferent nerves in the spinal animal does not cause in the ordinary conditions of experiment, any trace of hair erection. In the numerous experiments on the limb nerves,

no movement of the hairs was seen either before or after injecting strychnine, nor did the splanchnic nerve cause erection unless the electrodes were placed on it dangerously near the sympathetic trunk. Nevertheless it is not to be concluded that afferent nerves are in all conditions incapable of acting on the spinal pilo-motor centres. In three experiments stimulation of an upper lumbar nerve just under the edge of the longissimus dorsi muscle caused erection of hairs, twice confined to the lower lumbar and sacral region, and once to this and the tail region. In each experiment the pilo-motor effect was obtained at the end of an experiment and the blood-pressure was only about 30 mm. Hg when the cord was no doubt in a semi-asphyctic condition. In some cases I have found that stimulation of a lumbar or limb nerve in the stage of asphyxia in which the hairs are beginning to become erect will cause an increase of rate of erection in the hairs of the sacral and tail regions. On the whole I think that the pilo-motor reflex when obtained is due to a summation of asphyctic and afferent nerve stimulation. In any case, the reflex is useless for determining the degree of local action in the ordinary condition of a spinal cat.

Effect of Strychnine on Spinal Reflexes from the Limb Nerves.

Carotid blood-pressure.

The effect of strychnine[1] on reflex changes of blood-pressure in spinal animals has not been investigated by many observers. The most complete observations are the early ones of Schlesinger(6). Schlesinger found in the rabbit that whilst after section of the spinal cord, stimulation of the median nerve had no effect, a more or less large rise was obtained in 18 out of 31 experiments by stimulating the nerve after injection of strychnine. Kabierski and Heidenhain(8) mention incidentally that after strychnine has been given to a spinal rabbit, stimulation of the sciatic may cause a large rise of blood-pressure. In similar experiments Asher and Lüscher(13) found some, but only a small rise of pressure in the spinal rabbit. Pike(15) found no rise in the spinal cat on stimulating the sciatic after any dose of strychnine.

In the previous accounts of the action of strychnine in Parts I and II (18, 19) I have given instances in which the sciatic, after injection of a small amount of strychnine, caused a rise of blood-pressure (cp. Exp. 8, Part I and Exp. 2, Part II). In all the subsequent experiments made on spinal cats, a rise of blood-pressure was obtained by stimulating a hind

[1] Strychnine is used for strychnine nitrate.

limb nerve after strychnine had been injected, except in two or three in which the excitability of the cord—as shown by direct stimulation, or injecting strychnine—was greatly decreased.

The general effect of strychnine on the reflex rise of blood-pressure depends within narrow limits on the amount given. But the extent of the rise of blood-pressure in each stage varies widely in different cats. The variations are no doubt in part due to variations in amount of blood lost, duration of dissection, vigour of the animal and so forth. But the chief conditions which influence the extent of the rise of blood-pressure is I think hunger and digestion. As I have said, nearly all my experiments were made in the morning on animals fed the night before (p. 238), and that three experiments were made on animals fed two hours before they were anæsthetised. In the fed animals, the reflex rise of blood-pressure after strychnine was much greater and more constant than in the earlier experiments. It will be convenient to defer an account of the results in animals in full digestion, and give first those obtained in the much larger number of experiments on those in hunger and slight digestion.

(*a*) After a certain small amount of strychnine (·1 to ·2 mg.) which either is just sufficient to cause a slight rise of blood-pressure, or which is just insufficient to cause one, stimulation of a hind limb nerve will produce a greater rise than before, commonly one of 20 to 40 mm. Hg. On successive stimulation the rise decreases, but on injecting the same small amount the rise is again greater, and again falls with successive stimuli. The rate of decrease of effect varies. It depends partly on fatigue for it is faster if the stimuli follow one another quickly, and there may be some recovery if after two stimulations at an interval of half a minute, an interval of two minutes is left. It is partly due to decreased concentration of strychnine for a decrease in rise of blood-pressure still occurs if an interval of several minutes is left between the first and second stimulation, and it is less than after other injections if the first stimulation is delayed for several minutes. The extract given below (Exp. 1) is from one of the experiments in which the sciatic had no effect before strychnine was given, and in which there was an unusually rapid decrease in effect after a small dose of strychnine.

In the less numerous experiments on the effect of minimal doses of strychnine on the lower thoracic, upper lumbar and brachial nerves, similar results were obtained, but the increase in the rise of blood-pressure was less.

(*b*) After an amount of strychnine which produces an approximately

Exp. 1. Cat. Decerebrated and curarised.

Time in mins.	Blood-pressure mm. Hg		Rise of blood-pressure on stim. sciatic
0	43	Spinal cord cut at 3rd cervical, rise of 49 mm.	
		Tie and cut sciatic	0
		Stim. sciatic. Sec. coil at 10 cm.	0
4	39	Inject ·05 mg. strychnine* (jugular)	
	40	Stim. sciatic	Trifling waves
9	40	·05 mg. strychnine* (slight waves)	
	42	Three stim. of sciatic at intervals of about a minute	23, 0, 0
16	44	·05 mg. strychnine*	
		Sciatic as before	33, 3, 4
		Interval 3 mins.—sciatic—sec. coil at 9 cm.	20, 6
28	41	·05 mg. strychnine*	
	43	Stim. sciatic	32
		Later there were spontaneous rises of blood-pressure. Four injections of strychnine totalling 2·3 mg. were made	
60	52	Stim. lower end of severed spinal end for 10 secs.—a rapid rise of 108 mm. Hg	

* The blood-pressure curve remained smooth. There was a trifling slow rise of 1 to 2 mm. only.

maximal rise of blood-pressure (2 to 3 mg. sometimes less) most stimulations of the hind limb nerves cause a rise of blood-pressure of 4 to 8 mm. of Hg, whether or no an effect has been obtained before injecting strychnine, but some of the stimulations are usually ineffective. Subsequent injections of 2 to 5 mg. gradually reduce and finally abolish the reflex rise. Each injection is apt to cause brief paralysis. Since the injection of the larger amount of strychnine commonly sets up 3rd order waves, the effect of stimulation can often only be deduced with certainty by an examination of the whole tracing. A similar rise may be obtained by pinching the foot or tail, but I very rarely found any effect from tactile stimuli, viz. rubbing the hairs backwards and forwards.

Occasionally when the larger amount is injected, the effect is slight at first and gradually increases. Thus in one experiment the dorsal nerve

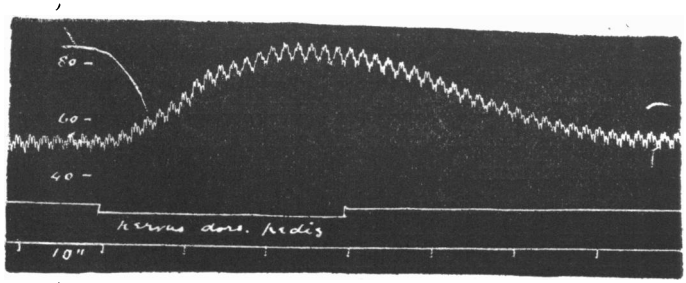

Fig. 4. Spinal curarised cat (3rd to 4th cerv.). Stimulation of the dorsal nerve of the foot 20 mins. after injection of 2 mg. of strychnine.

of the foot, stimulated at intervals after the injection of 2 mg. of strychnine, caused a steadily greater rise, until 26 minutes after the injection the rise was 34 mm. Hg (Fig. 4).

(*c*) There are two conditions in which stimulation of the sciatic is commonly coincident with a large rise of blood-pressure.

(i) A certain amount of strychnine, varying usually from ·2 to ·3 mg. according to the state of the circulation causes a large rise of blood-pressure but only after an interval of $1\frac{1}{2}$ to 2 minutes. When the rise is thus delayed, stimulation of the sciatic about a minute after the injection is nearly always followed in about 10 secs. by a quick and large rise of blood-pressure. Fig. 5 is an example of the effect. In this experiment

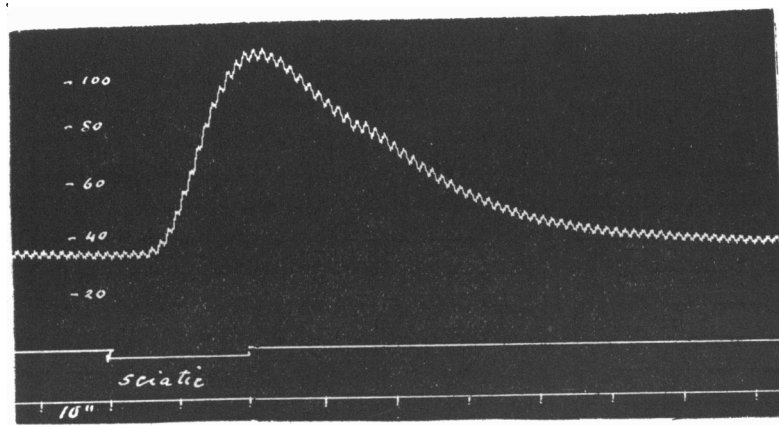

Fig. 5. Spinal cat, curarised. Sciatic stimulated 70 secs. after a second injection of 0·1 mg. strychnine. The following stimulation caused a rise from 39 to 58 mm. Hg.

the quick fall of pressure to nearly the original level is some, though not conclusive evidence that the rise was not simply a strychnine rise, for this ordinarily raises the pressure for some time above normal. It is not conclusive because relaxation of the intestinal vessels allows a quick fall of pressure; thus in the experiments in which the abdominal viscera were exposed in Ringer's fluid, curves of the type of Fig. 5 were obtained with strychnine.

(ii) The second condition in which the sciatic causes a large rise of blood-pressure (and subsequent rises of decreasing height) is when the strychnine causes a distinctly sub-maximal rise. Usually a sub-maximal rise occurs, as in (i), after a considerable delay. If it is followed by other spontaneous rises, the rises caused by sciatic stimulation are con-

siderably higher. But sometimes there is hardly any variation of blood-pressure in the intervals between the stimulations; thus in one experiment in which 1 mg. of strychnine after a delay of 70 secs. raised the blood-pressure from 48 to 178 mm. Hg, three successive stimulations of the sciatic caused rises from 142 to 220, from 102 to 150 and from 78 to 106 and in the intervals of stimulation there was no rise greater than 10 mm.

It is undeniable that in some experiments of this type, the rise which occurs on sciatic stimulation might be entirely caused by strychnine, but the examination of the whole of the tracings leaves me with no doubt that not infrequently the rise would not have occurred if the nerve had not been stimulated.

In the experiments made on the forearm nerves (median and ulnar), whilst the reflex rise of blood-pressure was considerable it was not so large as that obtained with the sciatic nerve.

Effect of digestion. In the three experiments made on animals in full digestion, attention was chiefly given to the effect of small amounts of strychnine. Large rises of blood-pressure were obtained in each experiment and the result was so clear, that it did not seem necessary to make further experiments. The rise was much greater and more constant than in the other experiments; it occurred in each of the stages, *a*, *b*, *c* of strychnine action mentioned above, but was especially convincing in stage (*a*) in which strychnine causes at most a slight gradual rise of blood-pressure. The following is an abstract of part of one of the experiments.

Exp. 2. Spinal cat, curarised. In full digestion. Small rises of blood-pressure varying from 2 to 9 mm. Hg were obtained by stimulating the sciatic, the rise was unaltered by the first injection of ·1 mg. strychnine; after the second injection of ·1 mg. the sciatic gave rises of 39 and 42 mm. Then:

Time in mins.	Blood-pressure mm. Hg		Rise of blood-press. from successive stim. of sciatic
0	44	0·1 mg. strychnine	
5	47	Sciatic	91*, 18, 3
15	43	0·1 mg. strychnine	
	43	Sciatic	81, 98
35		Excise intestine, stomach, pancreas and spleen	
42	55	0·1 mg. strychnine	
	60	Sciatic	80, 69, 41

Up to this point there were only trifling variations of blood-pressure in the intervals between the stimulations.

* This rise is shown in Fig. 6.

It will be seen in Fig. 6 that there is a distinct 2nd rise in the curve, suggesting liberation of adrenaline. The same form of curve, but of

relatively small height, occurred however later in the experiment after (evisceration and) clamping the adrenal veins. The first stimulation in

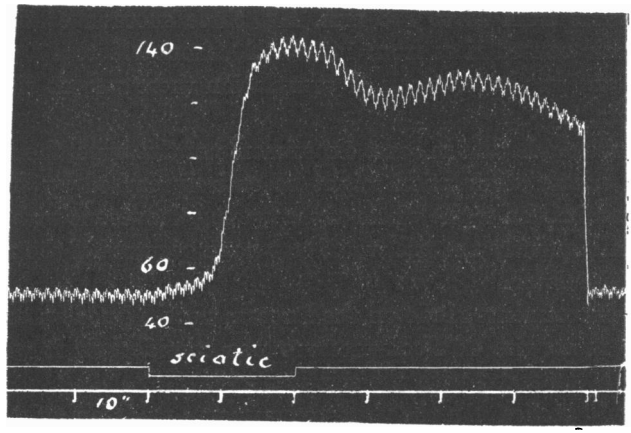

Fig. 6.

the other experiments gave curves of the same form, but the 2nd rise lessened with subsequent stimulations and in one disappeared (Fig. 7).

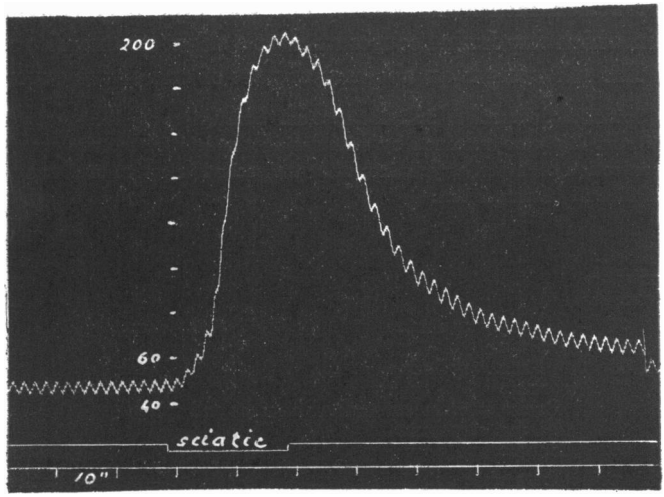

Fig. 7. Spinal cat (3–4 cerv.), curarised. The strychnine injected in this experiment was about that which usually itself causes large rises of blood-pressure, but there was no large rise except when the sciatic was stimulated. The figure shows the effect of the 5th stimulation when there was no secondary rise in the curve.

How far a discharge of adrenaline influences the form of the curve I have not determined. It depends no doubt, as in the intact animal, on the state of the adrenal glands. In animals with intact nervous system it has been shown by Stewart and Rogoff(20) that strychnine causes liberation of adrenaline, but a maximal rise of blood-pressure can be caused by strychnine after removal of the adrenals ((17), p. 157). It is not probable that liberation of adrenaline can be produced reflexly as a primary effect.

I have said (p. 243) that in hungry and slightly digesting spinal animals a considerable rise of blood-pressure may occur in recovering from a relatively large dose of strychnine. This was also found in one of the digesting animals. Five mg. of strychnine were injected (after 1·5 mg. in small doses). The rises of blood-pressure caused by successive stimulations of the sciatic in the following 20 mins. (during which the pressure sank from 109 to 78) were: 9, 13, 16, 30, 76.

From the results given above the following conclusions may be drawn. Strychnine in increasing concentration progressively increases the excitability of the spinal centres, so that the reflex rise increases until there is a spontaneous discharge of nerve impulses, and when this has occurred the reflex excitability greatly decreases and is gradually abolished with further increase of strychnine concentration. The several nerve cells are not simultaneously affected except by the larger amounts of strychnine and the successive rises of blood-pressure which occur are not, or only to a relatively small extent, due to discharges from the same group of cells, but to discharges from different cells. On these lines the varying result of afferent nerve stimulation found by others and by myself are intelligible, for the extent of the reflex effect depends on the exact stage of strychnine action at which the nerve is stimulated. Since in the non-digesting spinal animal after about 2 mgm. of strychnine the limb nerves cause a trivial rise of blood-pressure only, it is to be expected that sometimes, in consequence of a decrease of excitability of the spinal cord, not always avoidable by the methods used, no reflex rise would be obtained. The occasional gradual increase in reflex rise after 2 to 5 mg. of strychnine I take to be due to a decrease in the concentration of strychnine in the cells combined with a circulation sufficiently rapid to prevent the fall in spinal excitability which commonly occurs.

Relative effects of strychnine on visceral and cutaneous vascular reflexes.

Effects seen on injecting strychnine. In the spinal cat the injection of strychnine in an amount which causes a marked rise of blood-pressure causes usually a primary brief flush of the feet, followed by pallor. The flushing though distinct is not very great, it usually precedes the

rise of blood-pressure and gives way to pallor soon after the rise of pressure begins. At the height of the pressure rise—if this is considerable—the feet become dead white, even the small veins of the toes disappearing from view. As the blood-pressure falls, there is more or less return of the tint. In the experiments, several injections of strychnine were given beginning with a dose causing little or no rise of blood-pressure, and the maximum total dose was 5 mg. Probably the flushing would have been greater if the larger dose had been given primarily.

Observations were also made on the abdominal viscera exposed in warm Ringer's fluid. In the early period of exposure no distinct primary flush of the intestine was seen but there was distinct pallor when the blood-pressure rose; it was much less than that found (in other experiments) in the feet. In the later stages after exposure of the viscera (after about half an hour) in the warm bath, the pallor of the intestine accompanying a rise of blood-pressure lessens, and it may remain distinctly flushed during large rises of pressure caused by strychnine. In one experiment indeed the intestine remained red and seemed to become rather more flushed during a rise of blood-pressure from 80 to 180 mm. Hg.

Reflex changes in the colour of the feet. After a small amount of strychnine has been injected (·1 to 2 mg.) the sciatic (and any one of its main branches) causes easily observable changes in the colour of the feet. Whenever the sciatic causes a marked rise of blood-pressure, all the feet become pale, and if the rise is large, they become a dead white. The time of beginning of pallor, however, varies. There is commonly some flushing as a primary effect. In some cases the flushing is very trifling, and is not caused by every stimulation; this was so in two experiments on eviscerated animals, and the flushing was only slight in two experiments on hungry non-eviscerated animals; usually the pallor began with the rise of blood-pressure, continued during more or less of the fall of pressure, gradually returning to the previous state. In the three experiments on animals in full digestion primary flushing was marked and constant, its duration varied. Sometimes it began a little before the rise of blood-pressure, increased during the rise and began to decrease as the pressure began to fall. Sometimes it did not begin to decrease till the pressure was half way to its original level. Similar variations occur when the strychnine (in small amount) causes "spontaneous" rises of blood-pressure.

Since the vascular changes on sciatic stimulation occur in the fore feet as well as in the hind feet, the afferent nerves of the limb must be able to set in action the whole range of spinal vaso-motor nerve cells.

There is however evidence of a greater effect on the more posterior nerve cells. In the hind foot, on the opposite side to that on which the sciatic is stimulated, distinct though slight, flushing may occur without any change in the fore feet, and marked flushing when produced, occurs earlier and lasts longer in the opposite hind foot than in the fore feet.

A striking fact is that the vascular changes in the foot on the side on which the sciatic is cut are of the same nature as those on the side with sciatic intact and only differ from them in intensity and duration. Not only so, but they are of the same nature when the anterior crural nerve is cut at Poupart's ligament, the sciatic tied and cut at the sciatic notch and the central end of the sciatic stimulated. The common result of the stimulation is that all the feet flush, the contralateral hind foot most; when the blood-pressure has fallen a little, the fore feet begin to become pale; a few seconds later the homolateral hind foot begins to get pale, and a few seconds later still, the contralateral foot. The occurrence of flushing on the side with limb nerves cut indicates that it is a passive effect caused by constriction elsewhere. The greater flushing on the contralateral side indicates an active effect from vaso-dilator fibres. The eventual pallor on the homolateral side indicates contraction of the abdominal aorta or external iliac artery. But there are other possibilities and these I am investigating. I may mention that I have found essentially similar changes after evisceration combined with clamping of both adrenal veins.

Reflex changes in the viscera. The effect of strychnine on the abdominal viscera was not very striking. Any considerable reflex rise of blood-pressure caused pallor of the whole intestine, but when there was no considerable rise, the action of the sciatic appeared to be on the lower part of the intestine and on the pelvic viscera, and the action of the brachial to be on the stomach and duodenum, i.e. there was simply a slight increase of the effects obtained before strychnine was given. The anastaltic waves in the proximal colon increased greatly during the experiments, but how far this was due to exposure in warm Ringer's fluid and to a direct action of strychnine was not determined. It has been mentioned that Schlesinger(6) found that the brachial nerves had no effect on the rabbit's uterus after section of the spinal cord. He found, however, that when strychnine had been given, the brachial nerves caused strong uterine contraction.

Vascular Reflexes from the Splanchnic Nerve and the Effect of Strychnine on them.

Observations on the effect of the splanchnic nerve in the spinal animal appear only to have been made by Asher and Lüscher(13) and by Sherrington(16). In the rabbit Asher and Lüscher very rarely obtained any effect. In the cat Sherrington found that the splanchnic constantly caused a rise of blood-pressure. In his "Mammalian Practical Exercises"(16) a tracing (taken under his direction by a student) is given showing a rise of 9 mm. Hg, but he informs me that he has commonly found the rise to be greater than this—up to 25 mm. Hg.

In a few experiments made in 1919 I found, as had been found by Sherrington, that stimulation of the central end of one splanchnic nerve caused in each experiment a rise of blood-pressure (up to about 16 mm. Hg) and further that after 1–2 mg. of strychnine had been injected, the rise was increased to a variable extent (up to about 30 mm. Hg). When Dr Uyeno was working in the Laboratory in 1923, I asked him to repeat the experiments with a view of determining the constancy of the results. He made a number of experiments and from these most of the details given below are taken. The splanchnic nerve was exposed by dorsal dissection. Since the nerve by this method is isolated nearly up to its point of separation from the sympathetic trunk, care must be taken when stimulating it, to avoid spread of current to the trunk. Spread of current is shown by erection of hairs in the lumbar or in the lumbar and sacral regions. In most of the experiments the cat was decapitated; in five, the stomach, intestines, spleen and pancreas were excised. In three experiments after decapitation, the cord was again cut at the 3–4 cervical segment. The nerve was stimulated for about 20 seconds, two to four times before injecting strychnine, and a variable number of times after each injection. It may be mentioned that none of these experiments were made on cats in full digestion.

In the non-eviscerated cats, the splanchnic nerve gave a rise of blood-pressure with each stimulation. In 8 out of 15 experiments the rise was much the same, and was fairly constant with the successive stimulations, *e.g.* (*a*) 7, 6, 5·5 mm., (*b*) 7, 4, 6 mm., (*c*) 10, 8 mm. In four experiments it varied from 14 to 24, *e.g.* (*a*) 22, 18, 14 mm., (*b*) 14, 14, 22, 24, 16 mm. The highest rise obtained was 33 mm. The peripheral end of the splanchnic was for comparison stimulated in a few cases; it always caused a greater rise than that caused by stimulating the central end.

In 12 experiments the effect of the injection of strychnine (·5 to

2 mgm.) was to double approximately the splanchnic rise, but there was considerable variation in detail. (i) In most cases the rise became less with the successive stimulations; examples of this in different experiments are: (*a*) 36, 16, 10, (*b*) 22, 15, (*c*) 42, 12, 10, 8 mm. Hg. The rate of decrease depended partly on the interval allowed between the stimulation and was less if the interval were 2–3 minutes than if it were 45–60 seconds. (ii) In some cases, this progressive decrease did not occur after one or more of the early injections. Thus in one experiment after the second injection of 1 mg. strychnine, successive stimulations caused rises of 24, 18, 20, 26, 24, 20 mm. Hg. The difference no doubt depends mainly upon the rate of decrease of strychnine concentration in the blood. (iii) In most cases, each injection up to a total of 6 mgm.—the maximum given—caused again an increase in splanchnic effect, but in some cases increase was only obtained after the first, or after the first and second injection, the subsequent ones being followed either by no increase or occasionally by an absence of effect. The result was probably due less to a paralysing action of strychnine than to a decrease of excitability of the spinal cord in consequence of continued deficient circulation. (iv) In three experiments, in two of which the cord excitability was certainly decreased, the effect of strychnine was trivial, and there was only a slight and inconstant increase of the effect of splanchnic stimulation.

The results closely correspond to those of stage (*b*) of the action of strychnine on the effect of sciatic stimulation (cp. p. 242). After ·5 or 1 mg. one might expect the spontaneous contraction to be sometimes sub-maximal and that the splanchnic would then give a large rise. A large rise (60–70 mm.) was twice obtained, but there can be little doubt that with smaller amounts of strychnine the three stages present on stimulations the sciatic after strychnine would also be found on splanchnic nerve stimulation.

In the five eviscerated spinal cats, the reflex rise was on the whole less and more variable. The rises with successive stimuli were (*a*) 6, 8, 2, (*b*) 8, 4, 2, (*c*) 8, 4, 6, (*d*) 3, 0, (*e*) 2, 0, 0, 2, 6. It is, however, clear that the splanchnic nerve can cause vaso-constriction in the spinal cat in some area other than that of the abdominal viscera. The effects of strychnine on the reflex rise of blood-pressure were similar to those in non-eviscerated animals, but in two only of the experiments was the rise considerable (up to 40 mm.), and the effect of successive stimuli varied widely. In one experiment in which the blood-pressure fell to 40 mm. Hg, the increase in effect after strychnine, though fairly constant, was small. In the experiment mentioned above in which the rises of

blood-pressure on splanchnic stimulation before strychnine was injected, were 2, 0, 0, 2, 6 mm., those after injection were sometimes slightly greater, but as frequently stimulation had no effect.

The following abstract gives some details of an experiment in which the splanchnic caused a considerable rise of blood-pressure.

Exp. 3. Cat. Decapitated under chloroform and then curarised. Throughout the exp. the hairs on the back were observed; no erection occurred. Right splanchnic nerve tied and cut.

Time in mins.	Blood-press.		Rise of blood-press. in mm. Hg on stim. splanchnic. Spontaneous rises in brackets
0	96	Stim. splanchnic	18, 11
7		Spinal cord cut 3–4 cervical. Blood-press. rises to 192	
10	164	Splanchnic	8
11	159	„	7
14	104	„	33
15¼	102	„	24
17	84	1 mg. strychnine	
		Splanchnic	34, 66, (42), 38, (36), (36), 52, (20), 50, 38
41	60	Splanchnic	18, 8 (interval 4 mins.), 18
46	74	0·5 mg. strychnine	(74)
		Splanchnic	30, (50), 47, (48)
72	58	Splanchnic	36, 16
78	54	0·5 mg. strychnine	
		Splanchnic	46, 20, 48
95	46	(Cut splanchnic on opposite side stim. periph. end. Rises 66, 50)	
100	54	Splanchnic	10
101		0·5 mg. strychnine	
102		Splanchnic	12, 8, 10
		(Stim. periph. end. Rises 54, 54)	

The local action of the limb nerves shows that the afferent fibres of each spinal nerve end chiefly in the segments of the spinal cord near the region of their external origin. The greater effect of the splanchnic than of the limb nerves may then in part be due to its arising from a greater number of spinal nerves. But the main factor must be that it contains more of the special kind of afferent nerve fibres which gives rise to vascular reflexes.

I have also obtained a slight reflex rise of blood-pressure on stimulating the central end of the lumbar sympathetic, and Sherrington (private communication) has obtained a rise from the white rami of the ganglion stellatum.

Remarks.

It is clear that normally few afferent nerve impulses reach the spinal vaso-motor nerve cells. The great increase in the vascular reflex response

which strychnine is able to produce might be due to increased excitability of the nerve endings, or to increased excitability of nerve cells. On the whole it appears to me more probable that the action of strychnine is on the nerve cells. The intensity of the reflex response in regions remote from that stimulated, after strychnine has been injected, makes it probable that strychnine greatly increases the number of nerve cells which can be stimulated by afferent nerve impulses. That means that normally many nerve endings are unfunctional, and if, as assumed, the excitability of the nerve endings is not increased by strychnine, conduction of impulses from the nerve endings of the unfunctional nerve fibres to the nerve cells must normally be absent. The simplest explanation of the absence of conduction is that the nerve endings are less intimately connected with the nerve cells. Thus the stimulation of the nerve cells would depend on two factors—their excitability and the closeness of connection of the afferent nerve endings with them. On the same basis I should attribute the decreased vascular reflex from the spinal cord, which occurs in phylogenetic development as the higher centres gain more control, to a slight retraction of the nerve endings.

Whilst it is probable that spinal reflexes are normally unimportant, the great reflex rise of blood-pressure, which may occur after a certain small amount of strychnine has been administered, makes it equally probable that in pathological cases of increased spinal excitability they become of great importance.

A fall of blood-pressure on stimulating the nerves—even of the most trifling kind—was rarely obtained, and it could not with certainty be attributed to the stimulation. The fall of blood-pressure which others have found in the dog, is probably the result of a special development of the vaso-dilator mechanism in this animal.

As I have said above (p. 237) I do not think that the trifling nature of the reflexes obtainable in acute experiments is due to shock. If the reflexes obtained represent very nearly the normal reflex capability, it follows that the great reflex response which has been shown to be obtainable in chronic cases of spinal section, on the blood-pressure, on sweating and on contraction of the bladder are not due to recovery from shock. Head and Riddoch(21) in their very striking account of the reflexes obtainable in chronic cases of spinal transection in man adopt the theory that the increase in response is due to the cessation of inhibitory impulses proceeding from the cerebral hemispheres. There are two facts which I think are not accounted for by this theory, viz. the very retarded development of the reflexes and their greater development in the part of the spinal

cord a little below the section than in the more peripheral part. Head and Riddoch found that reflex sweating was much more profuse in the part of the body receiving sympathetic fibres from the upper region of the severed cord than in that receiving such fibres from the more peripheral region. The most probable cause of the increase of reflexes is I think that the degeneration of the cut fibres causes an increase of excitability in the nerve cells in which they end. Degeneration of peripheral nerves has been shown to cause increased excitability to drugs. The greater excitability of the tissues, as that of the spinal cord, is of gradual development and the greater number of fibres degenerating a little below the place of section of the cord than more peripherally might account for its greater excitability in the former region.

Note on the action of strychnine on autonomic nerve centres.

It has incidentally been mentioned above that afferent nerve stimulation after injection of strychnine has no reflex effect on the hairs, and no very obvious effect on the abdominal or pelvic viscera. Corresponding with this absence, or merely slight increase, of reflex excitability after strychnine has been injected is an absence of stimulation, or a merely slight stimulation, on its injection. It causes slight contraction of the bladder, and may cause some contraction or inhibition of the intestine, but it does not cause in the curarised spinal or decerebrate animal micturition or defæcation, nor any prolonged inhibition, or tonic contraction of the intestine. In the spinal cat I have not found that strychnine causes secretion of sweat, but my observations have been incidental; it is certain however that it may cause large rises of blood-pressure without any secretion. Pillcher and Sollmann(22) found that it caused contraction of the spleen, but the contraction was apparently slight. Acceleration of the heart in spinal cats generally occurs when strychnine causes a sudden rise of blood-pressure, but this appears to be due mainly to increased pressure acting on the heart, for in more gradual rises of pressure, the rate of heart beat is altered little or not at all. Whether the primary flushing which strychnine causes in the foot of the cat is due to stimulation of vaso-dilator sympathetic nerve cells I hope soon to decide.

Strychnine does apparently stimulate the sacral vaso-dilator nerve cells. To investigate this, a few experiments were made on decerebrate and curarised cats, the penis being freed from the prepuce and surrounding tissues. The injection of 2 to 5 mg. of strychnine caused marked swelling and protrusion of the penis. Subsequent injections (5 to 20 mg.) had a variable effect. One experiment was made on a dog.

In this the primary effect of the first dose was retraction of the penis, although the bucco-facial region flushed strongly.

In the anæsthetised cat, strychnine causes moderate primary dilatation of the pupil and other sympathetic eye effects. Section of the cervical sympathetic delays the action, suggesting that the primary effect is due to weak sympathetic stimulation.

Schlesinger(6) describes strychnine as causing strong contraction of the uterus in the rabbit. Apart from this possible exception (and the reaction in the rabbit may differ from that in the cat), a *strong* stimulating action of strychnine on spinal nerve cells is, in the cat, confined to those governing striated muscles and blood vessels.

On the autonomic centres above the spinal cord the stimulating action is also limited.

In the cat and dog, after extirpation of the superior cervical ganglion to prevent pupil dilatation by way of the sympathetic, strychnine does not cause contraction of the pupil, so that the pupillo-constrictor centre (tectal autonomic) is not appreciably stimulated.

An action of strychnine on some bulbar autonomic centres is open to doubt. It occasionally causes secretion of saliva, but commonly it does not; when secretion occurs it is possibly a reflex produced by the bitter alkaloid stimulating the taste buds. S. Mayer(4) considered that it stimulated the cardio-inhibitory centre. What he found was that with the rise of blood-pressure there was sometimes slowing of the heart. In decerebrate and curarised cats slowing of the heart is inconstant, it occasionally occurs after section of the vagi (and also in spinal animals) when there is a sudden rise of blood-pressure; at any rate the inhibitory action is slight. Here again the only strong stimulation appears to be of the somatic and vaso-motor mechanism.

The proof given by Wertheimer and Delezenne that strychnine stimulates the bulbar vaso-dilator centre I have mentioned in an earlier paper ((19), p. 157). In this statement I overlooked the experiments of Dubois (*C. R. Soc. Biol.* 1904, Pt I, p. 355) who found that flushing of the tongue of the dog caused by strychnine after injection of adrenaline was prevented by section of the lingual nerve.

Summary.

The observations except some of those referred to in paragraph 9 were made on curarised spinal cats. The animals were anæsthetised first with chloroform then with C.E., then either decerebrated, the vagi cut and the cervical spinal cord severed, or they were decapitated.

1. A trifling rise of blood-pressure of 1 to 4 mm. Hg can usually be obtained by stimulating the central end of any limb or trunk nerve. Occasionally the rise is somewhat greater. It is less constant in eviscerated than in non-eviscerated animals, and in hungry than in digesting animals. It is concluded that in normal body conditions afferent somatic nerves are capable of causing a trifling rise of blood-pressure as a spinal reflex.

2. A rise of blood-pressure is constantly obtained, as noticed by Sherrington, by stimulating the central end of a splanchnic nerve. In the experiments the rise varied from about 8 to 24 mm. Hg (once 33 mm.).

3. Stimulation of the central end of a hind limb nerve sometimes causes faint flushing followed by faint pallor in the hind feet without observable change in the fore feet. When the abdominal viscera are exposed in warm Ringer's fluid the hind limb nerves appear to cause slight pallor and other effects in the large intestine, and the brachial nerves to cause pallor in the stomach and duodenum. It is concluded that the reflex effect is restricted in area, but that it is not so restricted as to make it of importance in local circulation.

4. In all cases in which the excitability of the spinal cord is not greatly lowered, a reflex rise of blood-pressure can be obtained after injecting strychnine. The extent of the rise depends on the amount of strychnine. Most of the experiments were made on cats fed the night before. On these the following results were obtained. An amount of strychnine which caused only slight rise of blood-pressure usually enabled the sciatic to cause a rise up to 20–40 mm. Hg. An amount of strychnine not more than sufficient to cause a large rise of blood-pressure after a delay of a minute or more enabled stimulation of the sciatic or of the brachial nerves to cause a large rise of blood-pressure. In both of these stages, the rise decreased with successive stimulations. An amount of strychnine just sufficient to cause an approximately maximal rise of blood-pressure, enabled a somatic nerve, or the splanchnic, to cause a rise about double that obtained before strychnine was given. Further increase in the amount of strychnine decreased the reflex rise and eventually prevented its occurrence. In spinal animals in full digestion much greater rises of blood-pressure were obtained in all stages of increase, especially in the first.

5. After a small amount of strychnine, reflex changes in the colour of the feet are great. In hungry animals pallor of all the feet was the predominant effect, but sometimes there was some primary flushing, greatest in the hind foot of the side opposite to that on which the sciatic

was stimulated. In the animals in full digestion, primary flushing was greater and more constant, sometimes it continued during the whole period of rising blood-pressure and for a short time after the pressure had begun to fall. It was greatest and lasted longer in the hind foot on the opposite side to that on which the sciatic was stimulated. In all cases it was succeeded by pallor. In the foot of the same side the stimulation caused retarded and less primary flushing followed by maximal pallor although the anterior crural nerve as well as the sciatic was cut.

6. Any considerable reflex rise of blood-pressure after giving strychnine was accompanied by pallor of the whole of the exposed intestine, but after a certain time of exposure, large spontaneous rises of pressure occurred without appreciable pallor of the intestine. Reflexes on visceral movement were apparently only slightly affected by strychnine.

7. No reflex effect from the limb nerves or from the splanchnic was found either before or after strychnine on the hair or the sweat glands. The upper lumbar nerves in rare cases caused local erection of hairs, probably in consequence of an asphyctic increase of excitability of the spinal centres in the particular experiments.

8. The great reflex rise of blood-pressure obtainable after a small amount of strychnine has been injected makes it probable that in pathological cases of increased spinal excitability, spinal vascular reflexes are important. It is suggested that the increased response of certain autonomic spinal centres which occurs a week or more after section of the spinal cord is due to an increase of excitability in the nerve cells caused by degeneration of the descending nerve fibres ending in them.

9. No evidence was obtained that strychnine greatly increases the excitability of any autonomic nerve centre except the vaso-motor centres.

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