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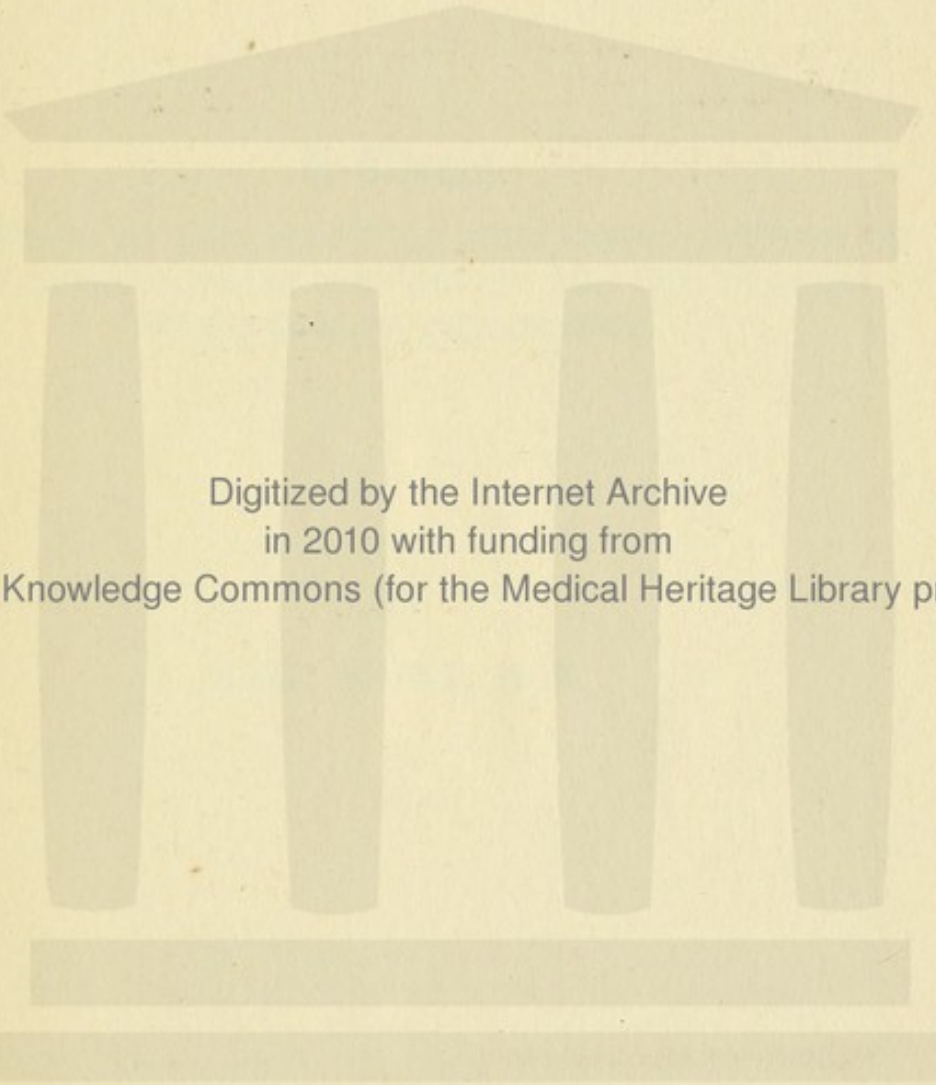

THE FALL OF BLOOD-PRESSURE RESULTING FROM THE STIMULATION OF AFFERENT NERVES.

A Thesis

PRESENTED TO THE BOARD OF UNIVERSITY STUDIES OF THE JOHNS HOPKINS UNIVERSITY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY.

BY

REID HUNT, A. B.

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THE FALL OF BLOOD-PRESSURE RESULTING FROM THE STIMULATION OF AFFERENT NERVES.

By REID HUNT, A.B. *Fellow in the Johns Hopkins University.*

(Six Figures in Text.)

Part I. Historical.

Two effects are commonly said to be produced by the stimulation of the central end of a sensory nerve—(1) reflex constriction of many of the smaller arteries, principally those supplied by the splanchnic nerves, and (2) a reflex dilatation of others, especially those of the skeletal muscles and of the skin[1]. As the effect of the former is usually greater than that of the latter, the result is a rise of arterial pressure. But a different result is often obtained, viz., a fall of arterial pressure. This latter result seems to have been first described by E. Cyon as following the stimulation of a sensory nerve of a rabbit under the influence of chloral.

The mechanism of the local reflex dilatation does not appear to have been very fully discussed; but the statements usually made seem to point to the conception, that the vaso-dilators of some parts of the body are in some way stimulated reflexly simultaneously with the vaso-constrictors of other parts.

Apparently no one has studied the question as to the areas in which the dilatation takes place when a fall of arterial pressure occurs as described above:—for example, whether the dilatation is general or is confined to certain localities; but several physiologists have made a study of the afferent nerves and the centres concerned. Cyon supposed a rise of pressure could be obtained reflexly only when the cerebral hemispheres were intact or normal; if they were removed or poisoned by chloral hydrate, a fall occurred. Dittmar[2], however, showed that the

[1] For references to the literature see Tigerstedt's *Lehrbuch d. Physiologie d. Kreislaufs.* Leipzig, 1893, pp. 518—529.

[2] Dittmar. *Ber. d. sächs. Gesellsch. d. Wiss.*, Math.-phys. Cl., 18. 1870.

pressure still rose, on stimulation of sensory nerves, after the complete removal of the hemispheres.

The first and apparently only thorough investigation of the afferent nerves concerned in this reflex was made by Latschenberger and Deahna[1]. From a study of the forms of the curves of blood-pressure during stimulation of various afferent nerves, from the fall of pressure obtained by long-continued stimulation of the sciatic, and especially from the fall following the removal of a clamp from the femoral artery, they concluded that from all the blood vessels of the body depressor as well as pressor nerve-fibres run to the vaso-motor centre. They thought further, that when the pressure in one vascular area was decreased (*e.g.* by clamping the artery) the pressor fibres were stimulated and a rise occurred, whereas, when the pressure is suddenly increased (as when the clamp was removed), the depressor fibres were stimulated and a fall of arterial pressure resulted. However, it was soon shown by Zuntz[2] that it was the anæmia of the tissues rather than the pressure in the blood vessels which caused the reflex rise of pressure. Then the failure of several experimenters to find another nerve like the depressor, stimulation of which invariably caused a fall of pressure, lead some physiologists to the view that there are no depressor fibres in the sense used by Latschenberger and Deahna[3], but that the fall of pressure sometimes obtained is due to the condition of the centre[4]. It is true that writers sometimes speak of "depressor" fibres in the sciatic and other nerves, and Bayliss[5] has recently put forward a theory of their action, but the possibility that the fall of pressure in these cases is due to changes in the centre was not excluded[6].

Howell[7] has recently published an account of experiments made by himself and some of his pupils, on the effects of cold upon the con-

[1] Latschenberger and Deahna. *Pflüger's Archiv*, XII. 157. 1876.

[2] Zuntz. *Pflüger's Archiv*, XVII. 404. 1878.

[3] Tigerstedt. *Op. cit.* p. 525.

[4] See Knoll. *Sitzber. d. Akad. d. Wiss. z. Wien*, Math.-naturw. Cl., 92, Abth. 3, p. 451. 1885. Also Foster, *Text-book of Physiology*, 6th ed. p. 345. 1893.

[5] Bayliss. This *Journal*, XIV. 317. 1893.

[6] After this paper had been written my attention was called to a section in the article by Bradford and Dean on the "Pulmonary Circulation" (This *Journal*, XVI. 67. 1894), in which they describe the effect of stimulation of the central ends of the intercostal nerves. They state that stimulation of the central ends of certain of these nerves is followed by a fall of pressure while that of the sciatic is followed by a rise, and argue from this that, as the vaso-motor centre is in normal condition, the fall can probably be explained only by supposing that there are two sets of fibres here—pressor and depressor.

[7] Howell, Budgett and Leonard. This *Journal*, XVI. 298. 1894.

ductivity of nerve fibres, in which he shows that, if a portion of the sciatic is cooled to near 0° C., and stimulated peripherally to this part, the result is a reflex fall of pressure. He suggests that there are depressor as well as pressor fibres present and that the former do not lose their power of conducting impulses at a low temperature as readily as do the latter.

Part II. The Afferent Fibres by which a Fall of Pressure is produced.

Method of experimenting. In addition to the method of cooling, other methods were employed to produce a reflex fall of blood-pressure; these will be described in their proper places. The animals used were cats, dogs, and rabbits and they were in all cases anæsthetized, by some method. The vagi were cut in most cases. The blood-pressure was taken from the carotid and recorded in the usual manner. In most of the experiments the nerve stimulated was the sciatic, but sometimes the saphenous, ulnar, median or anterior crural and occasionally other nerves were used. I shall consider first the stimulation of the sciatic, and then compare with these results the effects produced when the other nerves were stimulated.

1. Effect of Cooling.

The nerve was cooled in the manner described by Howell[1], viz., by drawing the central end of the divided nerve through the transverse tube passing through the angle of a V-tube; cold alcohol was circulated through the V-tube and so around the transverse tube containing the nerve. In this way the nerve could readily be cooled to 0° C. or lower. No attempt was made to determine the exact temperature of the nerve; the temperature given is that of the alcohol at the angle of the V-tube and as Howell showed, that of the nerve probably did not vary from this by as much as 1° C. The nerve was stimulated an inch or two below the tube with a weak interrupted current from a Du Bois Reymond coil. As the result varies with the kind of anæsthesia employed, it will be best to consider the different cases separately.

Brain Compression. This was produced by trephining, care being taken not to rupture the dura mater, and then carefully pressing a sponge or bandage, moistened with a ·6% solution of sodium chloride, into the cavity of the skull till anæsthesia was complete. Rabbits did

[1] Howell. *Op. cit.* p. 300.

not endure this operation very well and in cats, with the vagi divided, the curve of blood-pressure was sometimes very irregular and difficult to interpret. The method however often gave very satisfactory results.

Howell gives what may be considered a typical example of the reflex fall of pressure obtained by cooling and stimulating the sciatic when this method of anæsthesia is employed. I have nothing to add to his results. The effect is almost always easily obtained. The following experiment may serve as an example (see Fig. 1, *A* and *B*):

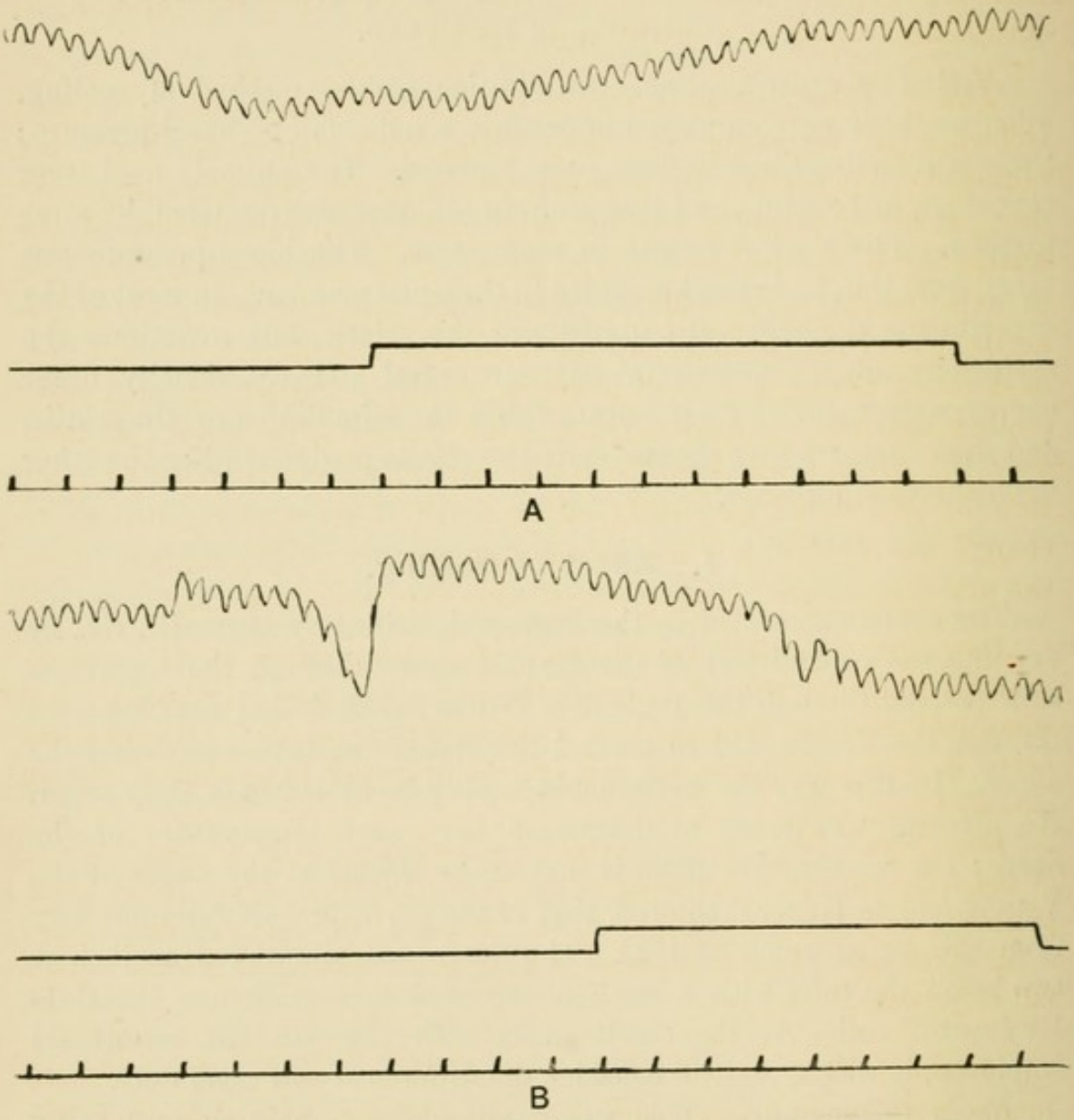

Fig. 1. Record from cat anæsthetized by brain compression. Vagi cut. Sciatic stimulated. "A" shows fall of pressure when nerve was cooled to $4\frac{1}{2}$° C. "B" shows rise of pressure when nerve was stimulated at 26°. Strength of stimulus the same in both cases. "B" is 1 minute, 50 seconds after "A." Tracing to be read from right to left. Time record in seconds.

Jan. 13th. Cat; vagi cut. Stimulation of the nerve with a current a little more than just perceptible to the tongue, with the nerve at 26° C. gave a rise of 38 mm. Hg. The nerve was cooled to 10° and again stimulated with the same current; there was no effect on blood-pressure or a minute rise. The cooling was now continued to 4½° C.; now stimulation was followed by a fall of 20 mm.; the pressure returning at once after stimulation ceased. Water at about 26° C. was now circulated around the nerve and the stimulus again applied 110 seconds after the former one. A rise of 28 mm. followed. Similar results were obtained in an experiment upon a cat anæsthetized by division of the crura cerebri.

Ether. Ether, alone or with other anæsthetics, has a marked influence in increasing the ease with which depressor effects are obtained. Very often in experiments in which this anæsthetic was used, a fall of pressure was the only result from stimulation of the sciatic at the temperature of the room. This was especially the case in experiments upon rabbits. With dogs and cats, however, if the nerve had been freshly exposed and the stimulating current was moderately strong, a rise of pressure usually occurred; in such cases cooling the nerve caused a marked fall during stimulation. If, however, the current was weak or if the nerve had been exposed for some time or stimulated frequently, either a fall of pressure resulted or no change was produced, either at the temperature of the room or when the nerve was cooled. Examples of such experiments are as follows:

Dec. 12th. Rabbit; vagi intact. With temperature at 23°, a weak stimulus caused a rise of 19 mm.; the nerve was now cooled to 15° and stimulated with the same current: a fall of 9 mm. resulted. Warming the nerve in this experiment did not restore its power to produce a rise on stimulation.

Dec. 13th. Dog; a.c.e. mixture. Stimulation, with a weak current, of the sciatic at the temperature of the room caused no change in the blood-pressure; with the temperature at 12°, however, the same current caused a fall of 10 mm. In this experiment weak stimulation alone did not cause a fall of pressure.

Acetone Chloroform (Trichloride of Acetonic Acid[1]). A few experiments were made on cats and dogs anæsthetized with this drug; the curves of blood-pressure were remarkably uniform, and a slight rise or fall was more conspicuous and less difficult to interpret than with many

[1] I am indebted for this drug to Prof. Abel, who has been using it for some time in his laboratory as an anæsthetic.

other anæsthetics. On the other hand, the vaso-motor centre did not seem to be very irritable and the reflex changes of pressure were not great. The results, however, were similar to those obtained with brain compression. The following will serve as an example.

May 10th. Cat, anæsthetized with 1 Gm. Acetone Chloroform. Vagi cut. Blood-pressure 75 mm. Hg., rising later to 100 mm. With temperature at 26° and secondary coil at 7 ctm. from the primary, a rise of 7 mm. occurred; the temperature was lowered to 4°: now stimulation with the same strength of current was followed by a fall of 7 mm. As the nerve was warmed again stimulation caused a rise; at 29°, coil 7 ctm., the rise was 20 mm.

Curare. Curare seems to exert an opposite influence to that of ether, *i.e.* it causes the pressor effects to be more marked. No fall of blood-pressure could be obtained by stimulating the cooled sciatic in curarized cats or rabbits when ether had been given or the brain compressed, or in dogs to which morphia and curare had been given[1].

In one experiment upon a cat with curare and brain compression, no fall of pressure could be obtained on cooling, but on injecting 3 c.cm. of a 10 % solution of chloral hydrate into the external jugular vein, stimulation of the sciatic readily caused a fall of pressure when the nerve was cooled to 10° C. or below.

In many cases, especially at the beginning of an experiment, the rise of pressure was followed soon after stimulation ceased, by a very marked fall. This result will be discussed later.

Ulnar and Median. A few experiments were made upon these nerves in dogs and cats; the same results were obtained as with the sciatic, viz. a rise at high temperatures and a fall at lower ones.

Saphenous Nerve. In rabbits and dogs a fall of pressure can be obtained from this nerve on cooling, as easily as from the sciatic; also in animals anæsthetized with ether or chloroform, a very marked fall sometimes results from stimulation. The saphenous nerve of the cat seems to differ markedly in this respect from that of the rabbit or dog. For in this animal a fall of pressure rarely occurred from stimulation of the saphenous whatever the anæsthetic, or the temperature or the strength of the stimulus. In the same individual cooling and stimulating the sciatic often gave a fall of pressure, while similar treatment of the saphenous was without effect. So, too, in animals anæsthetized

[1] Grützner failed to obtain fall of blood-pressure from cooling and stimulating the sciatic of a curarized dog. *Pflüger's Archiv*, XVII. 215. 1878.

with ether, the saphenous gave either a rise or no effect, while the sciatic often gave a fall of pressure. Thus there seems to be a real difference between this nerve and those so far considered. In this connection the statement of Knoll that a fall of pressure sometimes results from stimulation of most afferent nerves, with the exception of the splanchnic[1], is of interest; also the observation of Bradford[2] that a fall of pressure sometimes occurs on stimulating the intercostals.

2. Effect of stimulating the central end of a recently regenerated nerve.

A few experiments were made to determine whether, in the regenerating sciatic, any difference in the time of return of the different reflex vaso-motor functions could be observed, or, stating the problem in the terms of the hypothesis that there are two sets of fibres, pressor and depressor, whether one set regenerates earlier than the other. This work was suggested to me by some observations of Professor Howell's on the regeneration of vaso-motor nerves; he found that the dilators regenerate earlier than the constrictors.

The animals chosen for these experiments were, with one exception, cats; one sciatic was crushed by drawing a ligature tightly around it, high in the thigh; the wound was closed with aseptic precautions and the nerve allowed to regenerate. When signs of sensation and motion became apparent for some distance down the leg, that is, after the lapse of five or six weeks, the animal was experimented upon; both sciatics (the regenerating and the normal) were cut and their central ends stimulated alternately, and the effect upon the blood-pressure recorded on the kymograph. In all but one experiment there was distinct evidence that the depressor effect returned first; the exception being an experiment upon a cat made forty-eight days after the nerve was crushed. This was the longest period allowed to elapse between crushing the nerve and making the experiment and the part of the nerve stimulated gave the same results as the normal nerve, viz. a rise of blood-pressure. It is very probable that if the nerve had been cut lower down and stimulated, the usual result would have been obtained. A few details of some of the experiments will be given.

June 26. Cat. Left sciatic crushed 39 days previously. Anæsthesia was produced by brain compression and the two sciatics prepared for stimu-

[1] Knoll. *Sitzber. d. Akad. d. Wiss. zu Wien*, Math.-naturw. Cl., 92, Abth. 3, p. 449. 1885.

[2] Bradford. This *Journal*, x. 397. 1887.

lation. Stimulation of the left nerve with the coil at 8½ ctm., a weak stimulus, caused a slight fall of pressure; the coil was moved up to 7 and then to 4 ctm.; falls of pressure of 8 and 10 mm. respectively occurred. Stimulation of the right, *i.e.* the normal sciatic, with the coil at 8 ctm. gave a rise of pressure of 40 mm. These results were constant and obtained both before and after section of the vagi. (Fig. 2, *A* and *B*.)

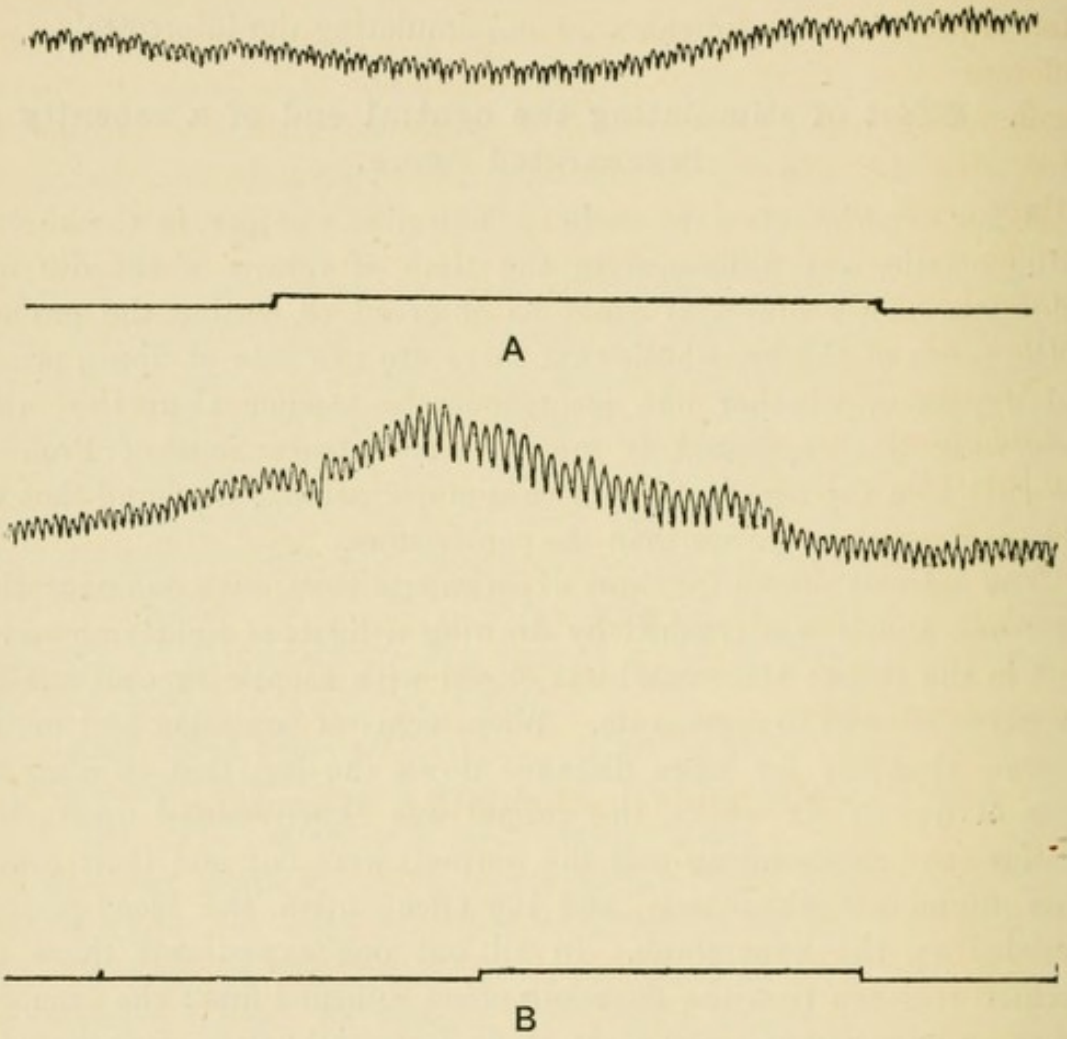

Fig. 2. Cat. Brain compressed. Vagi intact. Left sciatic crushed 39 days previously. "A" shows fall of pressure from stimulation of regenerating sciatic. "B" shows rise of pressure and slowing of heart from stimulation of normal sciatic. Tracing from right to left.

Dec. 12th. Cat. Left sciatic crushed 38 days previously. Anæsthesia produced by ether. Vagi intact. Stimulation of the normal nerve gave a rise of 16 mm.; the same current applied to the left caused a fall of 12 mm. The maximum fall of pressure in this case was obtained by stimulating the nerve immediately below the point where the ligature had been applied.

Another experiment shows a gradual transition in the effect upon the vaso-motor centre from stimulation of the nerve at points more and

more towards the periphery. When the stimulus was applied to a point near the wound there was a rise of pressure; a little lower, a fall occurred. As the nerve was stimulated still more peripherally the effect became less and less, and finally a point was reached where it seemed entirely unirritable,—at least as far as its influence on the vaso-motor centre was concerned. Another experiment showed the same difference between the normal and regenerated nerve in a slightly different way. In this experiment stimulation of both the normal and regenerating nerve caused a fall of pressure when the current was weak; the strength of the stimulus was now increased: the regenerating nerve continued to cause a reflex fall of pressure while the normal one caused a rise. Results entirely similar to the above were obtained in an experiment upon a dog in which one sciatic had been crushed 38 days previously.

An experiment was also made upon the saphenous nerve of a cat. Stimulation of the regenerating nerve 42 days after it was crushed, at, and just below the point where the ligature had been applied, caused a rise of pressure; when applied to a still lower point, stimulation was without effect. In no case did a distinct fall of pressure result from stimulation of this nerve, as was the rule with the regenerating sciatic. This is the result we should expect when we remember that a fall of pressure from stimulation of the saphenous is very unusual.

3. **Mechanical stimulation of muscles.**

Kleen[1] has shown that if a purely muscular stimulation be produced by kneading the muscles of a rabbit's leg, a fall of blood-pressure results; Brunton and Tunnicliffe[2] have obtained similar results. I repeated this experiment on cats and rabbits and found that here also the anæsthetic had a marked influence on the result.

With curarized cats, morphia also being given or the brain compressed, kneading the muscles of a limb invariably caused a fall of blood-pressure. The following will serve as an example.

Feb. 2nd. Cat. Morphia and curare; vagi cut. Kneading the muscles of the leg, from which the skin had been removed, caused a fall of pressure of 10 mm., after which the pressure slowly returned.

With brain compression alone, kneading the muscles usually gave a fall of pressure, but the results were not so marked or so invariable as

[1] Kleen. *Skandinav. Archiv f. Physiol.* I. 247. 1887.

[2] Brunton and Tunnicliffe. This *Journal*, XVII. 373. 1894.

with curare. With ether the results were still less marked; and one or two experiments on cats anæsthetized with acetone chloroform gave negative results. The fact that a fall of blood-pressure could be so easily brought about by kneading the muscles, if, at the same time, care was taken to avoid rubbing the skin, suggested that direct electrical stimulation of the nerves to the muscles, or of the muscles themselves, would also cause a fall. This supposition, however, was shown by experiment to be incorrect. The nerves investigated were branches of the sciatic and anterior crural, and subsequent dissection showed them to be, in large part at least, muscular; stimulation of these, with weak or strong interrupted currents, was always followed by a rise of pressure. Direct electrical stimulation of the muscles by plunging the electrodes into them also gave a rise, while kneading them caused a fall of pressure.

4. Weak electrical stimulation.

Knoll[1] remarks that he received the impression from his experiments, that a depressor effect was usually the result of a weak stimulation, while the pressor effect followed, as a rule, a stronger stimulus.

I often noticed the same difference; sometimes it was very marked. For example, in an experiment upon a cat anæsthetized by brain compression, stimulation of the sciatic with the secondary coil at 10 ctm. from the primary, caused a fall of 12 mm.; with the coil at 7 ctm., on the other hand, there was a rise of 16 mm.

5. Effect of repeated stimulation, of exposure, &c.

Latschenberger and Deahna[2] observed that after the sciatic had been stimulated repeatedly, a point was reached when a fall of pressure took the place of the usual rise.

According to their theory the pressor fibres fatigued earlier than the depressor. Their experiments were made upon curarized animals. I have often obtained the same results, but far more readily on animals anæsthetized by brain compression. The following experiments will illustrate this point.

Dec. 30th. Cat anæsthetized by brain compression. Stimulation of the sciatic nerve with a weak current caused, in the early part of the experiment,

[1] Knoll. *Op. cit.* p. 451.

[2] Latschenberger and Deahna. *Op. cit.* pp. 165—6.

a very considerable rise of pressure; soon however a strong stimulus was required to produce this effect, a weak one causing now a fall. After one stimulation with a weak current, with the temperature at 24° C., the fall was 24 mm.; the wound was then closed and the animal left undisturbed for an hour. The blood-pressure fell considerably during this time, but otherwise the condition of the cat seemed to have remained unchanged. At the end of the hour the sciatic was stimulated with the same strength of current and at the same temperature as before; the result was a rise of pressure of 38 mm.

It might be objected to this experiment that the long interval between the stimulations had permitted some change to occur in the centres themselves. A second experiment will therefore be described to which this objection cannot be made.

Jan. 10th. Cat; brain compression and light etherization. The right sciatic was exposed, but some difficulty was experienced in getting it properly adjusted in the cooling tube; consequently the nerve was exposed to the air for some time and rather roughly treated. Stimulation of this nerve with currents of moderate strength caused only a fall of pressure. The left sciatic was now quickly exposed and stimulated with a current of the same strength as that employed for the right nerve; a rise of pressure was the invariable result.

Unless we make the assumption that stimulation of the two sciatics may normally be followed by different results, this experiment can scarcely be explained otherwise than by supposing the rough treatment and exposure of the right sciatic to have made it incapable of conducting or developing pressor impulses as readily as depressor.

Another difference between the vaso-motor reflexes obtained from curarized animals, and from those anæsthetized by ether or brain compression, may be mentioned in this connection. It often happened that the rise of pressure, following stimulation of the sciatic of curarized animals, was followed, after stimulation ceased, by a very considerable fall. Later in the experiment, no such succeeding fall of pressure occurred although the rise was as great as before; indeed the pressure often remained above the previous level for some time. With animals under ether, a phenomenon opposite, in a certain sense, to this occurred; the first few stimulations caused a rise of pressure, while later only a fall occurred. Another kind of after-effect was sometimes observed on cats anæsthetized by brain compression. For example, in the early part of one experiment, no fall of pressure occurred after the rise from stimulation of the sciatic; later there was invariably such a fall of pressure.

These results will be referred to later in speaking of the action of curare and ether.

6. Effect upon the blood-pressure of closing and opening a vascular area.

Latschenberger and Deahna laid considerable stress upon the phenomena resulting from closing and opening a vascular area. As described above, they found that a rise of pressure followed the clamping of an artery, and a fall, greater than could be accounted for on purely mechanical principles, occurred when the clamp was removed. They attributed these results to the stimulation of pressor and depressor nerves respectively of the vessels of the area to which the arteries were distributed.

As far as I am aware no one has repeated the experiments with reference to the fall of pressure and it seemed desirable therefore to do so. I think the results obtained agree with those described by the above writers, but as they were not invariably obtained and were not marked, the experiments were not continued. The following will serve as an example.

Cat, anæsthetized by ether; the sciatic, anterior crural and saphenous nerves were cut on the right side; those of the left were intact. When the right common iliac artery was clamped, the pressure in the carotid rose 10 mm. and remained at that height till the clamp was removed, when it returned to just the level it occupied before. A rise of pressure would of course be expected when a tolerably large vascular area is suddenly closed. And further we should expect a greater rise to follow the closing of arteries which were dilated from section of their nerves, than from those whose nerves were intact. And this is what was found; for the immediate rise following the clamping of the left common iliac artery was extremely slight. In the course of a minute and a half the pressure rose, however, 6 mm. This rise cannot be explained on mechanical grounds since it did not occur on the sides where nerves had been cut. It is probably due as explained by Latschenberger and Deahna, to a stimulation of pressor nerves, not as they thought, by the collapse of the arteries, but by the local anæmia as described by Zuntz. The clamp was now removed from the left artery and another placed simultaneously upon the right; the rise of pressure in this case was but 5 mm. or one half as great as above. Latschenberger and Deahna observed an actual fall in such cases. The explanation of this is pro-

bably the one given by Latschenberger and Deahna; that is, that the sudden distention of the artery (or the sudden inrush of oxygenated blood, by which the local anæmia was relieved), stimulated depressor fibres and so the mechanical effect of simultaneously closing the right artery was, to a certain extent, counterbalanced.

This hypothesis is made more plausible by similar results obtained by a slightly different method, which seems less open to objection. As described above, the removal of the clamp from the artery on the side whose nerves were cut, was followed by a simple return of the pressure to the original level; removal of the clamp from the side with the nerves intact, was followed by a fall below the original level. In some cases the fall was as much as 13 mm. Section of the nerves on this side caused the difference to disappear.

7. **Negative results.**

In addition to the various forms of stimulation described above, two others were tried in the hope that some separation of the pressor and depressor effect might be obtained. They gave negative results, but I shall refer to them briefly.

Different rates of electrical stimulation. Rhythmic stimulation of the sciatic was tried with the thought that perhaps some such separation of pressor and depressor effect might be produced, as has been described for the peripheral constrictors and dilators by Ostroumoff[1] and especially by Bowditch and Warren[2], but the result was negative. The nerve was stimulated with an induced current; the current of the primary circuit was interrupted at different rates, from once in two seconds to sixty times per second. Only a rise of pressure resulted, the character of which was determined by the number and strength of the stimuli; the rise was very gradual with slow weak stimulation, but took place much more suddenly with stronger and more rapid stimulation.

Chemical Stimulation. It seemed possible that some chemical stimulus might be found which would have the effect of causing a fall of pressure when applied to an afferent nerve. A few salts, acids, and alkalis were therefore tried, but as yet no form of chemical stimulus has been found which seems to be capable of giving a depressor effect. As very little work has been done on the effect upon blood-pressure of

[1] Ostroumoff. *Pflüger's Archiv*, XII. 228. 1876.

[2] Bowditch and Warren. This *Journal*, VII. 432. 1886.

chemical stimulation of afferent nerves[1], it may be of interest to include, in the form of a table, my chief results.

The substances whose action was to be studied, were applied in equimolecular solutions to the central end of the divided sciatic by means of a camel's hair brush. After each application the chemical was washed off with a ·6 % NaCl solution, a small piece of the nerve cut off and another application made.

I. Feb. 13th. Cat, anæsthetized by ether. Blood-pressure 184 mm. Hg. The stimulus was allowed to remain on the nerve in each case for 25–45 seconds.

Stimulus	% sol.	Result
KCl	3·72	Rise of pressure of 11 mm.
Induced current		,, ,, (very slight)
KBr	5·74	,, ,, 10 mm.
KI	8·28	,, ,, 4 mm.
NaOH	1	,, ,, 6 mm.
KOH	1·4	,, ,, 10 mm.
HNO_3	1	,, ,, 10 mm.
H_2SO_4	1	,, ,, 15 mm.
Induced current (moderately strong)		0
HCl	1	Rise of pressure 7 mm.
I		,, ,, (slight)

Curare was now given and the stimulus applied to the saphenous nerve.

NaCl	5·84	Rise of pressure 12 mm.
KCl	3·72	,, ,, 14 mm.
NaOH	1	,, ,, 11 mm.
KOH	1·4	,, ,, 8 mm.
NaOH	1	,, ,, 11 mm.
KOH	1·4	,, ,, 10 mm.

The vagi were now divided and the stimulus applied to the central end of one of these nerves.

Induced current (moderately strong)		Fall of pressure 8 mm.
HNO_3	1 %	Rise ,, 24 mm.

II. March 28th. Cat, anæsthetized by ether. The experiment was made in the same manner as the above.

Stimulus	% sol.	Nerve	Effect on blood-pressure
$CaCl_2$	11·1	L. Sciatic	0
Induced current (weak)		,,	Rise (very slight)

[1] See Grützner. *Pflüger's Archiv*, LVIII. 71. 1894.

Stimulus	% sol.	Nerve	Effect on blood-pressure
$MgSO_4$	12	L. Sciatic	Fall, followed by slight rise
$MgCl_2$	16	,,	,, ,, ,,
Current (moderate)		,,	Rise of 14 mm.
$BaCl_2$		,,	Rise of 7 mm.
$KClO_3$	12·25	,,	Rise, followed by fall
HNO_3	1	,,	Fall, followed by rise
Current (moderate)		,,	Rise of 7 mm.
Na_2SO_4	14·0	L. Saphenous	
Induced current (moderate)		,,	Rise of 8 mm.
$ZnSO_4$	16·1	,,	Rise
$CuSO_4$	15·9	L. Anterior crural	Fall of 8 mm.
Induced current (moderate)		,,	Rise of 8 mm.
KOH	1·4	,,	Rise of $3\frac{1}{2}$ mm.
Coil		,,	Fall, followed by a rise
Curare was now given and the vagi cut.			
Induced current (strong)		R. Vagus	Fall of 8 mm.
NaOH	1	,,	Rise of 4 mm.
Induced current (weak)		,,	Fall of 11 mm.
,, ,, ,,		R. Sciatic	Rise of 17 mm.
$KClO_3$	12·25	,,	Rise of 16 mm. followed by fall of 24 mm.

These experiments though very incomplete bring out one point of interest, viz., the difference which is sometimes observed between chemical and electrical stimulation. Thus in the first of the above experiments the sciatic readily gave a rise of pressure on stimulation with various chemical agents while electrical stimulation was ineffective; in the second, on the other hand, the latter stimulus was the more effective. A 1% solution of HNO_3, for example, when applied to the sciatic in the former case, produced a rise of 10 mm., while a moderately strong electrical stimulus was without effect; in the second experiment, a solution of HNO_3 of the same strength, produced a slight fall of pressure, though a weak electrical stimulation was followed by a rise of 7mm. The difference is more marked in the case of the vagi. In both of the above experiments, electrical stimulation of various strengths invariably caused a fall of pressure, while HNO_3 and NaOH produced a rise. (See Fig. 3, *A* and *B*.) In one case the rise was 24 mm. In an experiment upon a dog a fall of pressure (11 to 12 mm.) followed stimulation of the vagus by both the induced current and HNO_3 (1% solution).

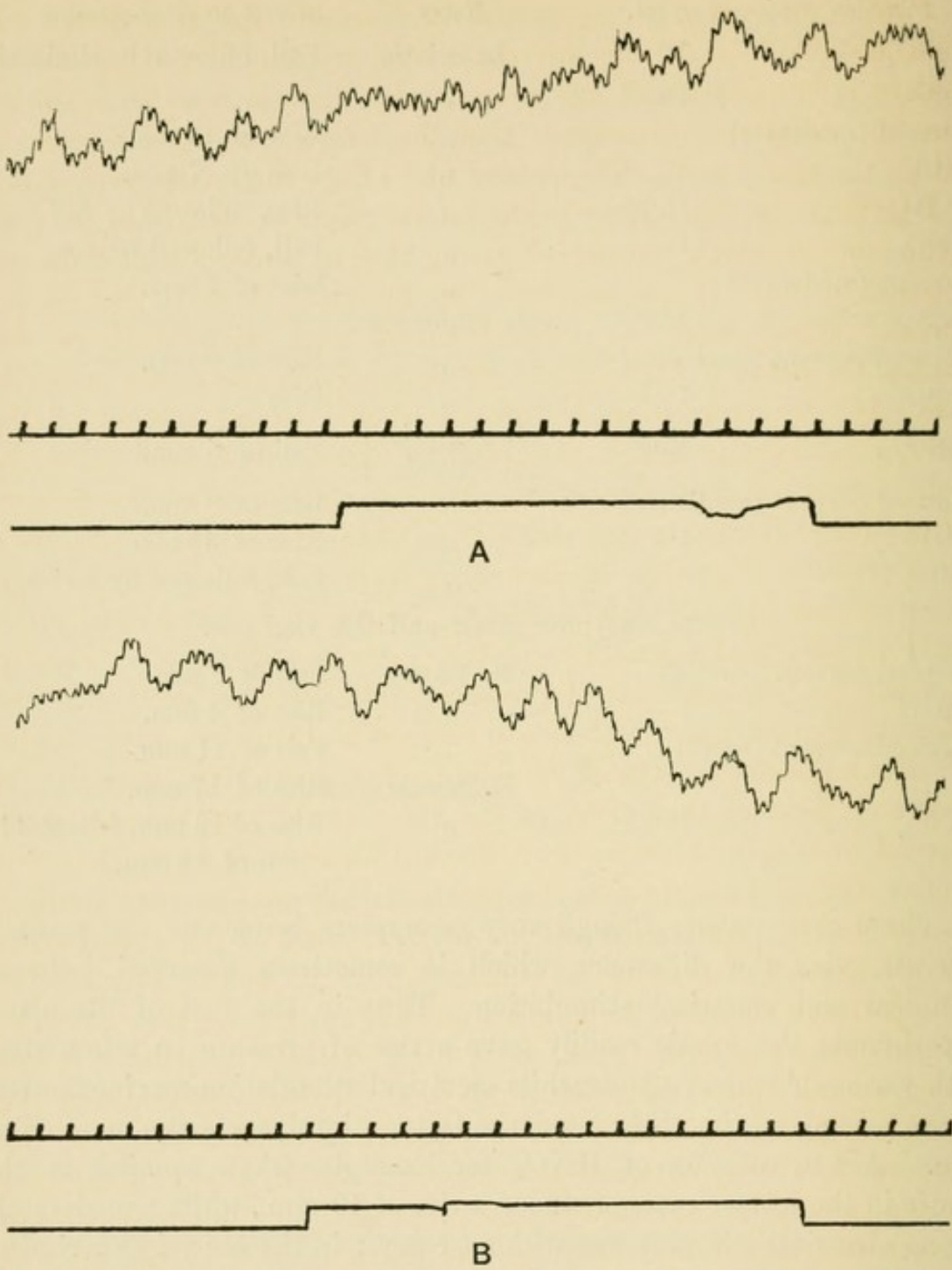

Fig. 3. Cat. Ether and Curare. Vagi cut. "A" shows fall of arterial pressure from stimulation of central end of vagus. "B" shows rise of pressure from stimulating vagus with HNO_3 (1%). Tracing from right to left.

So far as these experiments go, I think they show that the effects of both electrical and chemical stimulation vary with the condition of the animal, but that they vary independently. These differences do not seem to be entirely due to differences in the strength of the stimuli.

Path in the cord of the afferent fibres causing a fall of pressure. It seems possible that if the afferent fibres, by which a reflex fall of pressure is brought about, are anatomically distinct from those which cause the usual rise of pressure, that the former may have a separate path in the spinal cord. The pressor fibres from the sciatic were shown by Dittmar[1] to run largely in the lateral columns, that is, in the part of the cord in which the nerves giving rise to sensations of pain are supposed to run. It was suggested by Professor Howell that, as the depressor effects were so easily obtained from stimulation of the muscles, the afferent fibres might be those giving rise to the muscular sense. If this supposition is true we should expect section of the posterior columns, in which part of these fibres are known to run, to block, to some extent, depressor influences coming from the sciatic; and we should further expect stimulation of these columns to produce a fall of pressure. Neither of these suppositions, however, can be considered as satisfactorily demonstrated. In regard to the second point, it may be said that stimulation of the posterior columns gives usually, not a fall, but a slight rise of pressure. The effect of section of the posterior columns upon vaso-motor reflexes is likely to prove, under any circumstances, a difficult problem. For apart from questions of shock, and the fact that many of the fibres of the muscular sense are supposed to run in other parts of the cord, there is clear evidence that a reflex fall of pressure may be obtained through the cord itself at different levels. And, as a matter of fact, some of my experiments show a reflex fall of pressure on stimulation of the sciatic after section of the posterior columns, though this fall was not greater than could be obtained when the entire cord was divided. On the other hand it was noticed several times that after the spinal canal was opened and the posterior columns exposed, a fall of pressure from stimulation of the sciatic was less easily obtained than before. As the posterior columns were the parts most subjected to exposure and injury, this may perhaps be taken to indicate that they are the paths, in part, of the afferent impulses. In any case, it is interesting that after injuries to the cord, pressor effects are usually more marked, while after injuries to the brain the opposite seems to be the usual result.

[1] Dittmar. *Ber. d. sächs. Gesellsch. d. Wiss.*, Math. phys. Cl. 1873, p. 455.

Part III. On the local action of depressor nerve-fibres.

A number of experiments were made to determine, if possible, the vascular area in which the dilatation occurred which was the cause of the fall of arterial pressure described above.

It was obviously impossible, from the manner in which these experiments were made, to determine the effect on the vascular area corresponding to the nerves stimulated, for the efferent nerves were cut. However the case may be in the normal animal, it is clear that in these cases the dilatation occurred elsewhere than in the areas supplied by the afferent nerves. It was assumed that the area most probably involved in the dilatation was either the corresponding area of the other side or the splanchnic system, since this is known to play such an important part in most vaso-motor phenomena. Accordingly these two areas were investigated.

Method. At first sight the most satisfactory method of investigating this problem seemed to be the plethysmographic. Curare, however, is almost always necessary in such work, and this drug is, as has been shown above, distinctly antagonistic to a reflex fall of pressure from stimulation of sensory nerves. It is obvious, therefore, that the plethysmograph is not applicable to this work and accordingly other methods were tried; of these the determination of the venous pressure in different areas proved the most satisfactory and easiest of application.

The method employed was essentially that described by Bayliss and Starling[1]. An ordinary François-Franck cannula was used, into the horizontal limb of which a fine pipette was introduced so that it reached just into the neck of the cannula. The vertical limb was connected with a water manometer made of barometer tubing; a glass T tube was introduced into the rubber tube making this connection. When the vein was clamped, a stream of soda[2] could by this arrangement be led from the pressure bottle down into the neck of the cannula and out through the vertical limb of the T. The blood in the cannula could thus be washed out and all trouble from clotting avoided.

[1] Bayliss and Starling. This *Journal*, xvi. 162. 1894.

[2] The solution of soda used in both the venous and arterial cannulæ was the mixture of the carbonate and bicarbonate proposed by Klemensiewicz (*Sitzber. d. Akad. d. Wiss. z. Wien*, Math.-naturw. Cl. 94, Abth. 3, pp. 24—6, 1886). I have found this solution much more satisfactory than the solutions of $MgSO_4$ and Na_2CO_3 commonly employed in the laboratory. The proportions are as follows: Distilled Water 4000 c.c., $HNaCO_3$ 186 gm. Na_2CO_3 286 gm.

The veins in which the pressure was determined by this method were the portal, femoral, and saphena. For determining the portal pressure the cannula was introduced into the central end of one of the splenic veins. In the case of the femoral or saphena the cannula was put into a small branch, preferably into one joining the main trunk at a right angle. If a nerve in one leg was to be stimulated, it is to be understood that the cannula was in a vein of the leg of the opposite side.

Before describing the results of these experiments a word may be said concerning the interpretation of changes in the portal pressure. So little is known of the action of the constrictors of the portal vein —to what extent and under what circumstances, for example,—they are stimulated reflexly, that one must be very cautious in drawing conclusions from changes of pressure here.

Thus it is conceivable that both the arteries to the viscera and the branches of the portal vein should be constricted or dilated simultaneously. In this case there would be a rise or fall of arterial pressure with perhaps little or no change in portal pressure. On the other hand a rise of portal pressure might mean a dilatation of the arteries or a constriction of the portal vein and its branches in the liver. A fall of pressure might be ascribed either to a constriction of the arteries or to a dilatation of the veins. Perhaps there may be combinations of these effects. These possibilities show the difficulty of dealing with this subject; still the results are of value when simultaneous records of changes of pressure in other parts of the vascular area are taken.

Results. The results of these experiments on venous pressure may be stated very briefly. It was found that in nearly every case a fall of arterial pressure resulting from stimulation of the central end of the sciatic was accompanied by a rise of pressure in the femoral vein of the other leg. In the exceptional cases where no rise was obtained, there was either no change in venous pressure or only a slight fall. This result can not, under the conditions of the experiment, be a passive phenomenon, and I am convinced from a number of observations, that the respiratory reflexes can not be regarded as the cause of it. It seems to be due to an active dilatation of the vessels of the limb.[1]

The effect on the portal pressure was not so constant, but the result

[1] Brunton and Tunnicliffe (*loc. cit.*) have shown that when a considerable mass of muscle is kneaded there occurs along with the fall of arterial pressure a great increase in the outflow from the veins of the muscles kneaded.

was usually a fall. Whether this was due to active changes or was merely passive seems at present impossible to determine. Figure 4 shows these results in one experiment.

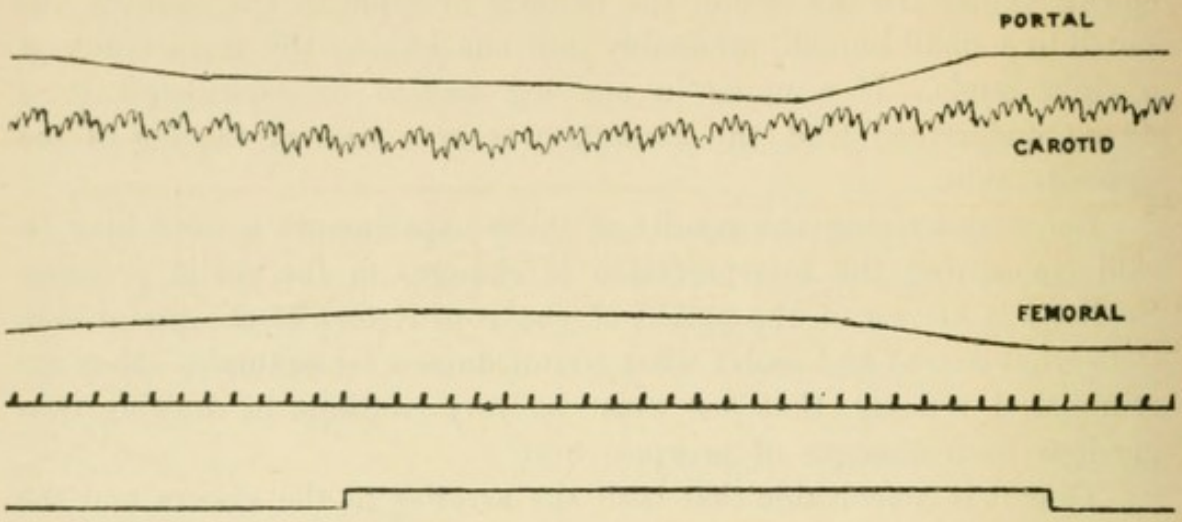

Fig. 4. Dog. Ether. Vagi intact. Fall of pressure in carotid and portal vein, and rise in femoral vein on stimulation of sciatic at 10°. All the curves have the same base line; the curves of venous pressure being drawn to indicate the pressure in mm. Na_2CO_3, the curve of arterial pressure in mm. Hg. The changes of pressure in the curves must be multiplied by 2 to obtain the absolute changes. Tracing from right to left.

All three curves are drawn to a common base line. The arterial pressure is expressed in mm. Hg.; the venous in mm. Na_2CO_3 solution. To show the absolute changes in pressure the distances of the curve must be multiplied by two. Both the fall of arterial and the rise of venous (femoral) pressure were slight in this experiment. In some they were 20 and 27 mm. Hg. and 20 and 30 mm. Na_2CO_3 respectively, the venous pressure being in such cases almost doubled. Similar effects upon venous pressure were observed when a fall of arterial pressure resulted from cooling and stimulating the ulnar or median.

It is interesting to compare with these results the effect on arterial and venous pressure of stimulating the central end of the vagus. This, as is well known, often causes a fall of arterial pressure which has been attributed to an inhibition of the vaso-constrictor centre and a consequent dilatation of the arteries, especially those in the visceral area. If this supposition is correct, we should expect to find little or no change in the pressure in the femoral vein, while the dilatation in the splanchnic area might cause a rise of portal pressure. This is, in fact, what was found in a number of experiments (see Figs. 5 and 6).

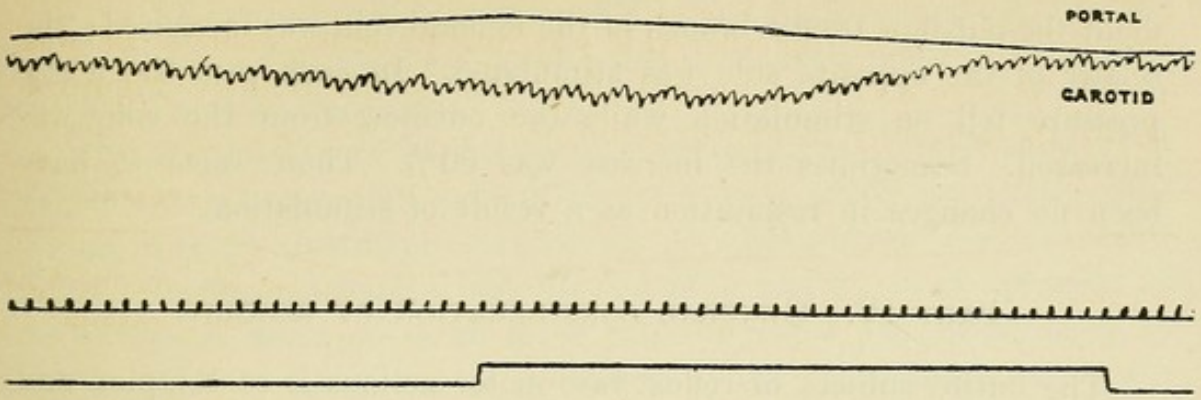

Fig. 5. Curves similar to above to show changes in portal and carotid pressure from stimulation of central end of vagus. Dog. Morphia and Curare. Tracing from right to left.

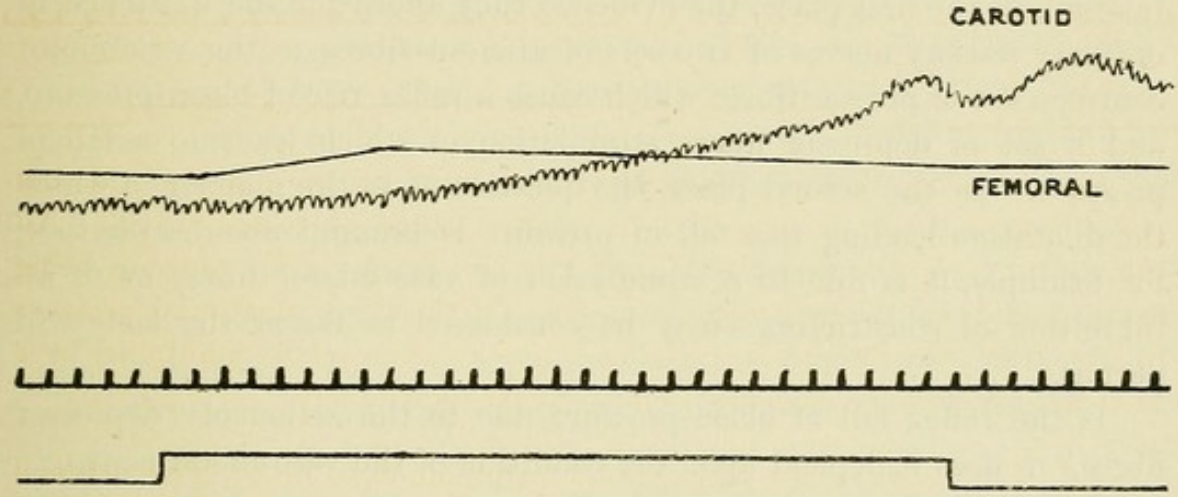

Fig. 6. Curves showing changes in pressure in femoral vein and carotid from stimulation of central end of vagus. Dog. Morphia and Curare. The arterial pressure returned from the fall slowly. Tracing from right to left.

The rise of portal pressure is often not very marked, but the fact that a large fall of arterial pressure may occur without any change in that of the femoral vein, indicates that the dilatation in such cases is largely elsewhere than in the limbs. It is probably of visceral origin. The fall of arterial pressure is sometimes accompanied by a fall in that of the femoral vein. This is probably a passive effect.

Two other experiments indicate that the dilatation occurs elsewhere than in the splanchnic area. The first of these was made upon a dog. The cœliac axis, the renal and the superior mesenteric arteries and the portal vein were ligated; cooling and stimulating the sciatic continued to cause a fall of pressure. In one case the fall amounted to 28 mm. The aorta was now tied above the inferior mesenteric and the radial stimulated. A fall of pressure was still obtained. In the other experi-

ment the out-flow from a branch of the femoral vein was measured; the sciatic of the opposite side was stimulated. In each case the aortic pressure fell on stimulation while the out-flow from the vein was increased. Sometimes the increase was 60%. There seem to have been no changes in respiration as a result of stimulation.

Part IV. General consideration of results.

The entire subject of reflex vaso-motor actions is so complex and so little understood, that the explanation of the above experiments is attended with many difficulties.

In considering the results of these experiments it will be best to take up, in the first place, the evidence they afford for the existence in ordinary sensory nerves of two sets of afferent fibres to the vaso-motor centre, a set of pressor fibres which cause a reflex rise of blood-pressure, and a set of depressor fibres, stimulation of which leads to a fall of pressure. In the second place, the question as to the manner in which the dilatation leading to a fall of pressure is brought about—whether, for example, it is due to a stimulation of vaso-dilator fibres or to an inhibition of constrictors—may be considered as far as the facts will permit.

Is the reflex fall of blood-pressure due to the action of "depressor fibres," or does it depend upon the condition of the vaso-motor centre?

As stated above, the second of these hypotheses seems to have gained most credit with physiologists, and there are many facts which indicate that the condition of the centres does modify profoundly the result of stimulating afferent nerves. Thus vaso-motor reflexes obtained from animals in which the cerebral hemispheres are intact differ from those observed when these parts are removed[1]—a fact which is probably explained by the condition of "shock" of the centres in the medulla, resulting from the operation. In the experiments recorded in this paper, however, where the nerve stimulated was subjected to the action of cold, or stimulation was applied to a regenerating nerve, no change can be supposed to have occurred in the centre; the action in these cases must have been upon the nerve fibres themselves. There are other cases, notably those in which certain anæsthetics or other drugs are used, where it is difficult to determine whether the centres alone are acted upon or whether the nerve fibres are involved. It will be best to consider these various cases separately.

[1] See Knoll. *Op. cit.* p. 456.

1. *Methods by which a reflex fall of blood-pressure can be obtained without any change being produced in the vaso-motor centre.*

The chief methods are as follows:

(1) Stimulation of afferent nerves when cooled, (2) stimulation of regenerating nerves, (3) stimulation of nerves which have been subjected to rough treatment or exposure, (4) employment of weak stimulation, (5) the mechanical stimulation of muscles. It is apparent at once that in none of these cases can the reflex fall of pressure be attributed to a change in the condition of the vaso-motor centre; the only part of the reflex arc altered by these agencies is the afferent nerves. As it is difficult to suppose that the same nerve fibres can at one time carry impulses having one effect, and at another impulses having exactly the opposite effect (the condition of the centre remaining the same), the simplest explanation of the fall of pressure in the above cases is that there are two sets of afferent fibres; we may suppose one set to make such connections with the centres that impulses passing up it cause a fall of blood-pressure, while the other carries impulses producing a rise.

That there are fibres which affect the vaso-motor centre in such a way as to cause a fall of blood-pressure, no one doubts, but they are usually supposed to come entirely from the heart and to run in the special "depressor nerve," or, if this is wanting, in the trunk of the vagus; in the latter case they are mixed with ordinary "pressor" fibres. If the existence of "depressor" fibres is admitted in this case, it seems much simpler to explain the depressor effects from other afferent nerves in a similar manner.

Moreover there is a more or less regular gradation in the effects upon the vaso-motor centre produced by certain nerves. At one end we have the depressor of the heart which, according to most observers, always causes a fall of blood-pressure; next the vagus of the dog and cat, which causes sometimes a fall, sometimes a rise of pressure, and the glossopharyngeal, which usually gives a fall; then come such mixed nerves as the sciatic, anterior crural, ulnar, median, the intercostals, and the dog's and rabbit's saphenous, from which depressor effects are obtained usually by special means; and finally we have the cat's saphenous and the splanchnic, which very rarely under any circumstances, give a reflex fall of pressure on stimulation. It seems almost necessary to suppose that the fibres of these various nerves make different connections with the vaso-motor centre or centres; if this is admitted, then we must admit that the fibres are different in the

sense in which we are using the word, that is, they constitute two different physiological varieties of afferent fibres.

The only alternative hypothesis which presents itself would be somewhat as follows. We might suppose one nerve fibre to be connected with both a dilator and a constrictor centre; and perhaps we might further imagine that a weak stimulus could reach or excite one centre more readily than the other, owing to a difference in irritability. In such a case the result of stimulating the afferent fibre would be largely determined by such factors as the strength and nature of the stimulus and the condition of the centres. But such a hypothesis would not explain why, when all the other conditions are the same, a depressor effect is obtained so much more readily from one nerve, *e.g.* the sciatic, than from another, *e.g.* the splanchnic. Here again we should have to suppose a difference in the central connections, the fibres of one nerve, for example, making closer connections with one centre than do those from the other nerve. And the same argument would apply with equal force to the difference between the effects of a purely cutaneous and a purely muscular stimulation, the former producing a rise, the latter a fall of blood-pressure.

From these considerations it seems impossible to avoid the conclusion that the afferent nerve fibres which cause a reflex fall of blood-pressure are anatomically distinct from those which cause a rise of pressure.

So far nothing has been said as to the exact manner in which the separation of pressor and depressor effects are produced in the cases where the nerve stimulated has been subjected to cold or exposure, or is regenerating. Granting that there are two sets of afferent fibres making different connections with the vaso-motor centres, we may suppose that a fall of pressure under the above circumstances is produced in one of the following ways.

In the first place, we might suppose that the impulses started in both sets of nerve fibres by stimulation are merely weakened by the above influences; and if it is further supposed that the dilator centre is more irritable than the constrictor centre, then a point might be reached at which the former only was able to respond to the weakened stimulus. It is well known that different medullary centres do differ in their irritability; the respiratory centre, for example, responds to stimuli too weak to affect the vaso-motor centre and, as has been described above, a weak stimulus applied to a nerve often causes a fall of blood-pressure, while a stronger causes a rise.

But there are several facts which indicate that the weakening of the impulses can play but a subordinate part in the cases under discussion. For example, a much greater fall of pressure can be obtained when the nerve is cooled and stimulated, than can be obtained by the use of a weak stimulus alone. Also stimulation of a regenerating nerve may produce, with the fall of blood-pressure, marked respiratory and cardiac reflexes, which indicate that the stimulus could not have been very weak.

We are therefore led to the alternative hypothesis as to the mode of action of the above-mentioned agencies in separating the depressor and pressor effect, namely, that when the nerve is cooled or is subjected to exposure, the pressor fibres lose their power of conducting impulses more easily than do the depressor, and that in the case of a regenerating nerve the latter class of fibres grow down or become functional earlier than do the former.

This explanation of the action of cold is the one proposed by Howell, who gives also several similar instances of the differential action of cold upon different nerve fibres combined in a common trunk. As regards regenerating nerves, there are already a number of facts which indicate that the fibres in a nerve trunk regenerate, as well as degenerate, at different rates. Thus, as was mentioned above, Howell finds that when the sciatic is cut and the ends sutured together, the vaso-dilators regenerate earlier than do the vaso-constrictors; Ostroumoff[1] showed that the vaso-constrictors degenerate more rapidly than do the vaso-dilators, and Mott[2] has recently stated that there is evidence to show that the afferent fibres in the spinal cord degenerate at different rates after section of a posterior root.

2. *Action of anæsthetics and of curare.* It is well known that when some anæsthetics, notably chloral and chloroform, are employed, the usual rise of pressure is often replaced by a fall, while when curare is given, a reflex rise is easily and constantly obtained.

The exact nature of the action of these drugs has not been determined, but the usual belief is that the drugs affect the nerve centres. This explanation seems very probable, when it is remembered that nerve centres are in general more sensitive to the action of drugs than nerve fibres; and that some of these anæsthetics, for example chloroform, cause a fall of pressure, due most probably to a partial paralysis of the vaso-constrictor centre. Still the possibility of a "differential action,"

[1] Ostroumoff. *Pflüger's Archiv*, XII. 228. 1876.

[2] Mott. *Brain*, Part I, 1892, p. 2.

to some extent at least, upon the afferent fibres, is not disproved. A few experiments made by applying some of these drugs (chloral, curare, and morphia) directly to the nerve trunk, or by injecting them into it with a hypodermic syringe, gave negative results as far as any change in conductivity or irritability was concerned. But such experiments show little, for the conditions were very different from those which exist when the drug is carried by the blood and the entire length of the nerve is exposed to its action. Ether, applied to the nerve, blocked the afferent impulses, but no separation of pressor and depressor effects was observed[1].

In this connection may be mentioned again the "after-effects" on the blood-pressure of stimulating afferent nerves, especially in animals poisoned by curare or anæsthetised by brain compression. As was described above, the rise of pressure so obtained is often followed by a marked fall. On the hypothesis that in afferent nerves there are two sets of fibres leading to the vaso-motor centre, we may suppose that both are excited simultaneously when the nerve is stimulated, but that the depressor fibres have a long "after-effect"; hence the fall of pressure after the stimulation ceases. This supposition would be similar to the one by which Roy and Adami[2] explain the vagus effects upon the heart which occur after the cessation of the stimulation of afferent nerves (the heart being accelerated during stimulation), and to Meltzer's[3] theory of the after-effects on the respiratory centre from stimulating the central end of the vagus, according to which the inhibitory fibres exert their influence during, and the inspiratory after, stimulation. This after-effect on the blood-pressure often occurs only in the early part of experiments on curarised animals. When the fact is remembered that curare seems to diminish the irritability of the depressor mechanism in general (or to increase that of the pressor mechanism, so that when both are thrown into action the latter predominates), the disappearance of the after-effect may be taken to indicate that this

[1] That curare has a marked effect upon the terminations of sensory nerves seems scarcely open to doubt. Heidenhain and Grützner (*Pflüger's Archiv*, xvi. 54—56, 1877) showed that often a slight stimulation of the hair of a curarised rabbit produced a much greater rise of blood-pressure than a strong electrical stimulus applied directly to the nerve and, as was shown above, a greater fall of pressure could be obtained by kneading the muscles of a curarised animal than from one simply anæsthetised; in fact a fall of pressure can usually be obtained in this manner from a curarised animal, while cooling and stimulating the nerve are usually ineffective.

[2] Roy and Adami. *Phil. Trans.* vol. 183 B, 259. 1892.

[3] Meltzer. *New York Medical Journal*, 51, p. 59. 1890.

mechanism is rapidly paralyzed or easily exhausted when this drug is employed. Though it is not definitely proved, the simplest supposition is that the drug acts directly upon the centres; thus the vaso-dilator centre may be supposed to be affected before the constrictor centre. That the constrictor centre may also be affected is shown by the absence of a reflex rise of pressure after a large dose of curare.

What appears to be the opposite effect, viz., a rapid paralysis or exhaustion of the pressor mechanism, is often observed in experiments on etherised animals, especially it seems upon rabbits. In such experiments the effect of the first two or three stimulations may be a rise of pressure, after which only a fall can be obtained. The chief factor in diminishing the irritability of the pressor mechanism is doubtless the direct action of the ether upon the constrictor centre, though the possibility of some action upon the afferent nerve fibres can not be excluded. That the latter supposition is possible seems to be shown by the fact that, after one sciatic, for example, has been stimulated till a reflex fall of pressure is obtained (a rise of pressure having followed the stimulations at first), stimulation of the nerve on the opposite side will cause, for a short time, a rise of pressure. This may be taken to indicate a weakening of the power to conduct impulses on the part of the pressor fibres of the nerve, or, on the other hand, to show that when the constrictor centre is partially paralyzed by the ether, some of its parts are still able to respond, for a time, to impulses coming up the pressor fibres after other parts have been completely exhausted by stimulation. The question which of these suppositions is correct, as well as the entire problem of a differential action of drugs upon the afferent fibres, must be left, for the present, undecided.

The nature of the reflex vaso-dilatation resulting from stimulation of the sensory nerves. The data for determining the manner in which reflex vaso-dilatation is brought about, whether by an inhibition of constrictors or by a stimulation of dilators, or by both agencies, are too few to make speculation of much value. But it at least seems very probable, that the mechanism concerned when the fall of pressure results from stimulation of ordinary sensory nerves, is different from that called into play in the dilatation resulting from stimulation of the depressor or of the vagus. In the former case the dilatation occurs to a much greater extent in the muscular system, and to a less extent in the splanchnic area, than is the case with the latter nerves. Another point of difference is the effect of curare in the two cases: while this drug usually makes it difficult or impossible to obtain a fall of pressure from stimulating the sciatic and

similar nerves, it seems to have little or no effect upon the reflex fall from stimulation of the depressor or vagus. Both these points of difference are readily explained, if we assume that the dilatation following stimulation of the depressor or the depressor fibres in the vagus is due to an inhibition of the constrictor centre, while that following stimulation of the sciatic and similar nerves is due to a stimulation of the dilator centre, since in a fall of pressure produced by the latter method we should expect the dilatation to occur chiefly in the muscular system where the dilator fibres predominate, while if the fall of pressure resulted from an inhibition of constrictor fibres we should expect the dilatation to occur mainly in the great splanchnic area where the constrictor fibres predominate. So also the action of curare in the two cases is explained on the above assumption, since it is well known that this drug in the usual doses increases the irritability of the vaso-constrictor centre, and we should therefore expect that it would not prevent the occurrence of a dilatation due to an inhibition of the constrictor fibres as we assume to be the case with the depressor nerve; whereas curare, according to Gaskell[1], Eckhard[2] and v. Frey[3], diminishes the irritability of the dilator fibres and should therefore tend to destroy or weaken a dilatation due to a reflex stimulation of the dilator fibres as we assume to be the case in the fall of pressure caused by stimulation of the sciatic, etc.

The different effects obtained from stimulation of various nerves in animals in which the blood-pressure has fallen as a result of the administration of ether or chloroform, or after exhausting operations, are also more easily explained by this view. Some of my records show that while the blood-pressure was high, stimulation of the vagus caused a marked fall of pressure, that of the sciatic a rise; when, however, the pressure had fallen after the administration of ether or the opening of the abdominal cavity, stimulation of the vagus no longer caused a fall of pressure, while there was often a marked fall from stimulation of the sciatic. If we suppose, therefore, that the fall of pressure from stimulation of the vagus is due to an inhibition of the constrictor centre and that after etherisation, exhausting operations etc., this effect disappears in consequence of a partial paralysis of the vaso-constrictor centre, the continuance, and indeed augmentation, of the depressor effect upon stimulation of the sciatic under these conditions can scarcely be referred to an inhibition of the constrictor centre, since this is apparently in a

[1] Gaskell. This *Journal*, I. 273. 1878—9.
[2] Eckhard. *Beiträge z. Anatomie u. Physiologie*, VII. 75. 1876.
[3] v. Frey. *Ludwig's Arbeiten*, II. 89. 1876.

condition of depressed irritability. Hence the alternative view, that the fall of pressure is due to a reflex stimulation of the dilator fibres, seems more probable in these cases also[1].

If we adopt this view it would be better to use the word 'depressor' in its original sense, *i.e.* to denote all afferent nerve-fibres producing dilatation by inhibiting the constrictor centre; and to use some other term, such as "reflex vaso-dilator" (which was employed by Howell), in those cases where the fall of pressure is produced by the stimulation of dilator fibres.

Summary of results.

(1) A reflex fall of blood-pressure was obtained upon stimulation of the sciatic and other mixed nerves by the following methods.

(*a*) Stimulation of nerves which had been subjected to the action of cold.

(*b*) Stimulation of regenerating nerves.

(*c*) The use of weak stimulation.

(*d*) The mechanical stimulation of nerves ending in muscles.

(2) In none of the above cases can the result be attributed to an abnormal condition of the vaso-motor centre.

(3) There is very strong evidence for the view that there are "depressor" or "reflex vaso-dilator" fibres in the sciatic and similar nerves.

(4) When a mixed nerve is cooled or is subjected to exposure, these fibres retain their power of conductivity longer than do the "pressor" fibres; when the nerve is cut and sutured, they regenerate earlier than do the latter.

(5) Anæsthetics and curare have a marked effect upon the ease with which a reflex fall of pressure is obtained; ether, chloroform and chloral are favourable, curare unfavourable, to its occurrence.

(6) The action of these drugs is probably largely upon the centres; the above-mentioned anæsthetics probably paralyzing the constrictor, curare the dilator centre.

(7) The fall of pressure from stimulation of the sciatic and of similar nerves is of a different nature from that resulting from stimulation of

[1] Bayliss (This *Journal*, xiv. 322. 1893) supposes that the fall of pressure following stimulation of the depressor nerve or the depressor fibres in the vagus is due mainly to a stimulation of the dilator centre, while the similar fall from stimulation of the anterior crural is due mainly to an inhibition of the constrictor centre, but it is difficult to discover in his paper from what evidence he draws this conclusion.

the depressor or vagus; in the former case the dilatation occurs largely in the limbs and curare is distinctly unfavourable to its occurrence; in the latter case the dilatation occurs to a much less extent in the limbs and curare does not seem to materially affect the ease with which it is obtained.

(8) The fall of pressure following upon stimulation of mixed nerves is probably due to a reflex stimulation of dilator fibres.

(9) It seems desirable to apply the name "depressor" only to those fibres which inhibit the vaso-constrictor centre and to use "reflex vaso-dilator" for the fibres exciting the vaso-dilator centre.

In conclusion I desire to express my sincere thanks to Prof. Howell, at whose suggestion this work was undertaken and to whom I am indebted for much aid and many valuable suggestions.

VITA.

The author of this thesis was born at Martinsville, Ohio, in April, 1870. He was prepared for college in the public schools of Ohio and in the preparatory department of Wilmington College. After spending a year in the Ohio University, he entered the collegiate department of the Johns Hopkins University in 1888. He received the degree of A. B. in June, 1891. The year 1891–92 was spent in study, partly in the Johns Hopkins University and partly in the University at Bonn. Returning to the Johns Hopkins, he acted as Assistant in Histology and Physiology 1892–93, and in Physiology 1893–94. In June, 1894, he was appointed Fellow in Physiology and was reappointed in June, 1895.

QP111 H91

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The fall of blood-pressure ...

QP111 H91