SOME REACTIONS OF SURVIVING ARTERIES.

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Method. The arteries for these experiments were obtained from freshly killed animals, except in the case of human arteries, which were obtained from a limb amputated from a living subject. From the freshly killed animal the arteries were transferred to oxygenated Ringer's solution at a temperature of about 35° C., in which they were kept till transferred to the Ringer's solution in which the experiments were performed.

The experiments were performed as soon as possible after the excision of the arteries, though it was found that, when precautions were taken for preserving the arteries at a constant and suitable temperature, their power of reaction to stimuli was retained without appreciable impairment for several hours after excision.

The Ringer's solution was thoroughly oxygenated by allowing oxygen to bubble through it for half an hour with periodical shakings.

A fresh supply of Ringer's solution was used for each experiment, and was maintained at a temperature of 35° C. throughout. The greatest care was taken to ensure that all the essential parts of the apparatus were kept free from extraneous contamination; the arteries were not touched by the hand, all the necessary manipulations being carried out by means of clean forceps and other instruments. The arteries, from which the rings were cut, before each experiment were cleanly dissected and freed from the surrounding connective tissue.

The apparatus used (Fig. 1) consisted of a glass beaker *G* containing a known quantity of the saline solution. This was supported by a wooden disc resting on the flanged lip of a metal water jacket *F*, so that the beaker was immersed in the circulating water contained in the water jacket. Protruding through a hole cut in the wooden disc was a

thermometer, which recorded the temperature of the circulating water. The water entry into the water jacket was provided by a pipe projecting from the lower part of the water jacket, connected by a length of rubber-tubing *I* with a copper coil *L*, fixed over a Bunsen burner. Water from a tap entered the lower end of the coil through the tubing *M*, and left at its upper end. The circulating water left the water jacket through a pipe projecting from the upper part on the opposite side to that on which it entered. The temperature of the circulating water, as of the saline solution within the beaker, could be maintained at any desired point by adjusting the rate of flow and the flame.

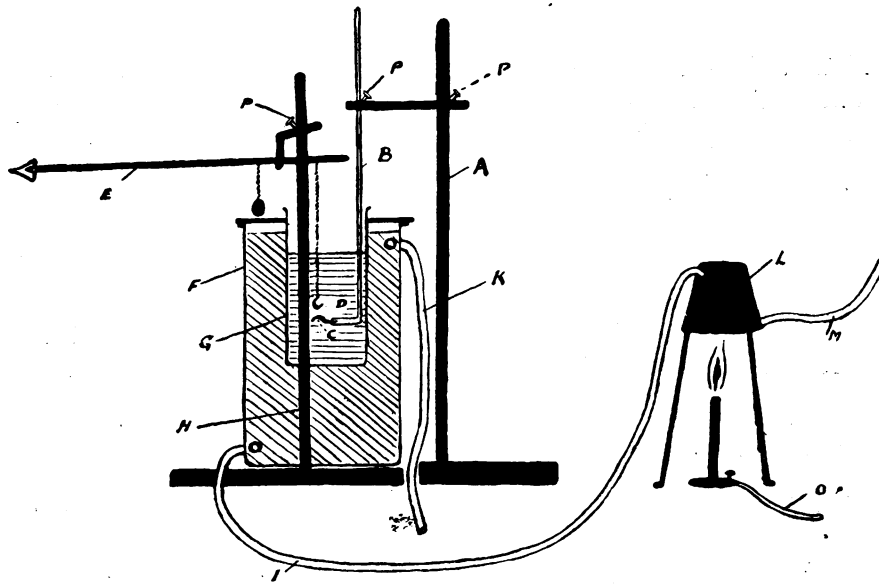

Fig. 1. *A*, rigid stand. *B*, glass rod. *C*, platinum hook. *D*, platinum hook. *E*, writing-lever. *F*, water-bath. *G*, beaker. *H*, upright. *I*, *K*, *M*, *O*, tubing. *L*, water-coil.

Supported by the cross-arm of a rigid metal stand *A* was a vertically placed glass rod *B*, the lower end of which was bent at a right-angle and carried a platinum hook *C* with its concavity facing downwards. This glass rod could be moved up and down and fixed at any desired height by the screw *P*, so that the lower end, carrying the platinum hook, could be immersed in the saline solution and held firmly. Another platinum hook *D* with its concavity facing upwards was

suspended by a silk thread from the short arm of a writing lever *E*, which was supported by the cross-arm of a second rigid stand *H*. Suitable balancing weights were hung from the near end of the long arm of the writing lever.

The method employed was that of O. B. Meyer: freshly cut rings of artery, about 2 millimetres in width, were used for each experiment, and were suspended in the saline solution between the two platinum hooks, sufficient tension to keep the silk thread taut being supplied by the balancing weights suspended from the writing lever. The drum was made to revolve slowly, 1 centimetre of the blackened surface passing the writing point in 42 seconds.

Drugs in solution were applied to the artery by instilling the fluid into the saline solution from a glass pipette fitted with a rubber bulb. Gaseous stimulants were applied by allowing the gas to bubble through the saline solution. Stimulation by variation in temperature was brought about by raising or lowering the temperature of the circulating water within the water jacket. Except in those experiments in which the dose of the stimulant is definitely stated, it is to be understood that the dose instilled was about $\frac{1}{2}$ c.c. in all cases in which liquid stimulants were applied. As the containing vessel held about 50 c.c. of fluid, the concentration of the drugs after dilution was roughly as follows: adrenalin 0·001 %, barium chloride 0·1 %, pituitary extract 0·1 %, alcohol 1 %, sparteine 0·01 %, tyramine 0·01 %.

It was found that the temperature of the saline solution could be made to remain constant within the limits of one degree.

Most of the arteries used were obtained from sheep and oxen, though a few experiments were performed with human arteries and with arteries obtained from goats and rabbits. In all, 201 experiments were performed; the results of eight of these were discarded, as in these instances it appeared doubtful whether the artery was in a condition to react to the various stimulants. In the remaining 193 experiments there appeared to be no reason to doubt that the arteries were reacting naturally.

Variation in temperature. MacWilliam(1) described the reactions of arteries to changes in temperature, and showed that very different results were obtained when the artery was in a state of contraction at the beginning of the experiment and when it was relaxed. In his experiments, however, he appears to have made no attempt to keep the arteries in a condition at all approximate to that obtaining within the living body: indeed the greater number of his experiments appear

to have been performed on arteries which had been previously frozen, or placed in olive oil, and in many cases kept for 24 hours or longer after the death of the animal from which they were removed. His chief result was a fairly constant "heat-contraction," occurring at or about 60°–65° C. This, however, as MacWilliam points out, would appear to be due not to muscular contraction, but to the elastic and connective tissue elements of the artery, since coagulation of muscle takes place at 45°–48° (Kuhne). Meigs(2) states that there is no connection between the shortening of plain muscle and coagulation of protein.

I performed eight experiments under this heading. The temperature of the saline solution was raised by degrees from about 12° C. to 55° or higher. The results were constant in the case of the carotid (Fig. 2), intercostal, cerebral and coronary arteries, showing in all cases a

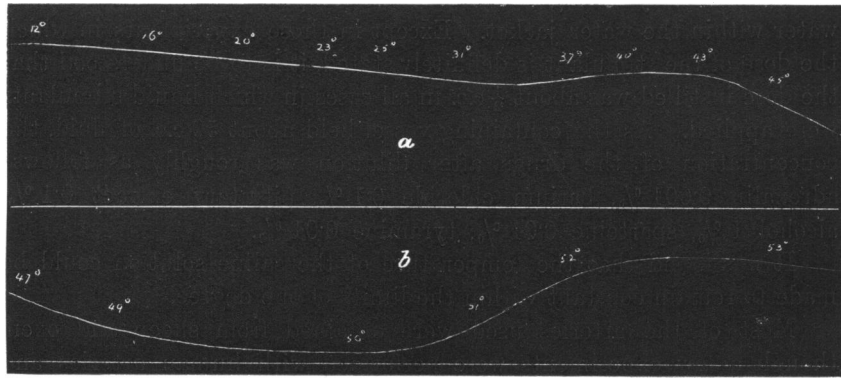

Fig. 2. Ring preparation of sheep's carotid. Shows the effect of alteration in temperature in degrees Centigrade. *b* follows on *a*.

preliminary slight relaxation of tonus which at or about 25° gave place to a slight and transient recovery of tonus, which in its turn gave place to a further relaxation; this increased progressively up to 45° or 50°. If the temperature was raised beyond this point, a further slight contraction was noticed, occurring at or about 60°, the "heat-contraction" of MacWilliam.

In the case of the gastric and hepatic arteries the results were similar to those just described, with this difference that the first recovery of tonus was not in evidence. The whole behaviour of these

arteries gave one the idea that they are more sluggish in their reaction than those mentioned above.

These experiments show that a rise in temperature produces relaxation in the arteries, with or without a slight recovery of tonus, which is but temporary, at a point slightly below that of normal blood-temperature: also that at a temperature higher than that at which coagulation takes place a contraction occurs which cannot be due to muscle coagulation. The latter effect is especially marked in vessels containing much elastic tissue.

Carbon dioxide. It has been known for a long time that the products of metabolism, produced by the activity of an organ, cause dilatation of the blood vessels of that organ. Barcroft and Dixon(3) conclude that carbon dioxide produces dilatation of the coronary artery.

I performed five experiments with this reagent, the results of which were uniform in showing that the arteries react to it by dilatation even with a liberal supply of oxygen. This result, however, was more marked in the case of the carotid and gastric (Fig. 3) than in the case

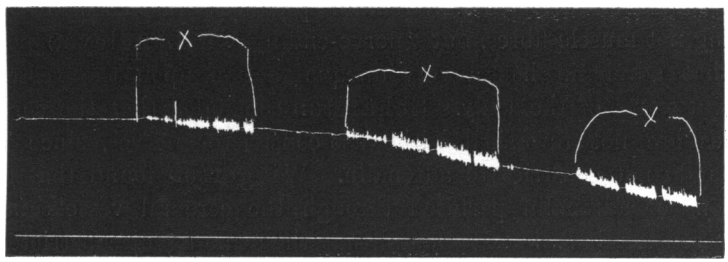

Fig. 3. Ring preparation of sheep's gastric artery: at the indicated crosses CO_2 was bubbled through the solution.

of the coronary artery. The dilatation lasted as long as the carbon dioxide was passing through the Ringer's solution, and as soon as the carbon dioxide was cut off the dilatation perceptibly diminished, though it did not cease. When the dose of carbon dioxide was repeated exactly the same phenomena were observed. Since the effect produced on the coronary and on the systemic arteries is the same, although their innervation is different, the results show that the vaso-dilatation induced by carbon dioxide is brought about by the action of the gas upon the muscle tissue of the artery wall, and not upon nerve-endings.

Alcohol. Dixon(4) in a résumé on the subject concluded that alcohol in moderate doses produces dilatation of the superficial vessels,

but if the dose is large, slight constriction of the internal vessels, followed by dilatation. He concluded that the action is partly central and partly peripheral. Kobert(5) stated that dilute solutions of alcohol have little effect on the renal vessels.

I carried out five experiments with alcohol, the arteries used being the carotid, gastric and coronary. The results were uniform, showing a slight and transient constriction, followed by a slightly more pronounced dilatation. The effect was of the same nature in the case of each artery, suggesting an action on the muscle tissue and not on the nerve-endings. The effect was, however, very small. The direct action of alcohol upon the arteries is one of dilatation: this may be preceded by a transient and inconsiderable constriction: as, however, both effects are very small, it would seem that the main action of alcohol on the blood vessels is not peripheral.

Adrenalin. Schäfer and Oliver(6) first showed the constricting action of supra-renal extract on the blood vessels. Brodie and Dixon(7) showed that adrenalin had no constricting effect when perfused through the lungs though this has been denied by Plumier(8) and Wiggers(9). They concluded also that adrenalin produces vaso-constriction by exciting not muscle fibres, but "nerve-endings[1]." Langley(10) pointed out that adrenalin has a very unequal action upon the vessels in different parts of the body. Schäfer(11) concluded that the coronary arteries are not furnished with vaso-constrictor nerves, since these vessels do not constrict to adrenalin. Wiggers(12) found that dilute solutions of adrenalin perfused through the cerebral vessels *in situ* causes constriction: he also found that the same agent constricted the coronary and pulmonary arteries. Dixon and Halliburton(13) found that perfusion of adrenalin through the cerebral vessels, the brain being removed from the skull, causes slight dilatation. Langley(14) observed that adrenalin has a specific power of stimulating plain muscle and gland-cells: that only those muscles are stimulated which are supplied with sympathetic nerves: and that the reaction to adrenalin is similar to that produced by stimulation of those nerves.

I performed 34 experiments with adrenalin, and from these the following results were obtained:

A well-marked constriction was produced in the case of the carotid,

[1] I have added inverted commas in order to draw attention to the fact that it is not necessarily upon nerve-endings, in the generally accepted sense of the term, that adrenalin exerts its effect, but upon the "myoneural junction" or the "receptive substance" within the cell (Langley).

facial, auriculo-temporal, anterior tibial, popliteal, gastric, hepatic, splenic and renal arteries. The constriction became evident after a very short latent period. The constriction was abrupt in onset, the writing point giving a tracing which rose suddenly at an angle approaching 90° with the horizontal. The height of the contraction was soon reached, and the artery remained for a long time in a state of increased tonus; indeed it was a remarkably rare occurrence for the constricted artery to show any sign of relaxation during the time occupied by a complete revolution of the recording drum, a period of about half an hour. In the case of the splanchnic vessels the onset of constriction was not quite so abrupt as in the case of the other systemic vessels, and the latent period was in many cases somewhat longer.

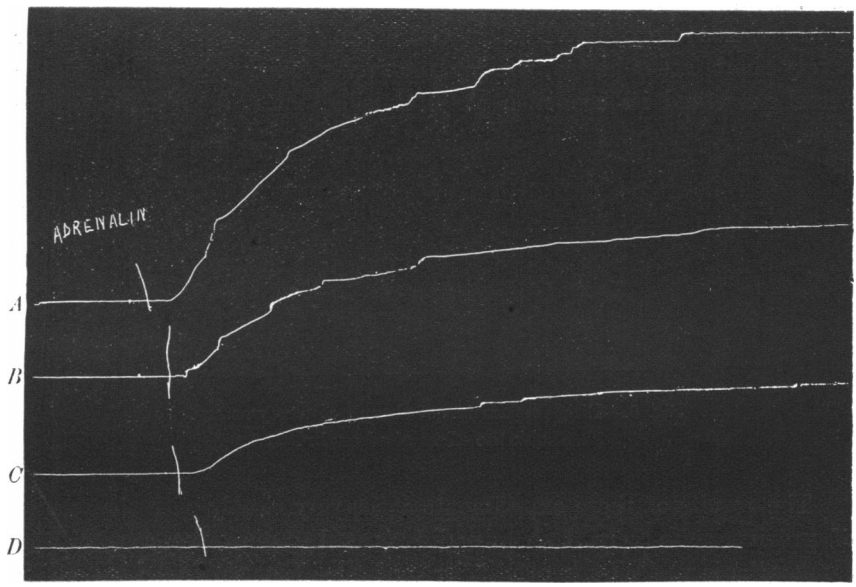

Fig. 4. Ring preparation from rabbit's pulmonary artery: at the indicated marks adrenalin was applied. *A*, is from the main stem, *B*, the primary branch, *C*, at the root of the lung, and *D*, within the lung.

The amount of constriction produced in the case of the intercostal artery was extremely small. Apart from this degree, the reaction of the intercostal artery was in all respects similar to the reaction of the other systemic arteries.

In the case of the pulmonary artery, whilst a certain part of the vessel standing outside the lung was definitely constricted, the artery contained within the lung tissue showed no reaction to the drug.

A secondary series of experiments with adrenalin was carried out on the pulmonary artery. That the application of adrenalin to the main trunk of the pulmonary artery causes constriction is well known. My results are shown in Fig. 4. It is there seen that a ring taken from the main stem of the artery showed a decided constriction; that a ring taken from the primary branch showed a less marked reaction; that a ring taken from the artery at the root of the lung showed hardly any effect, and that a ring taken from the arterial tree within the lung itself gave no reaction. Evidence of rhythmical contraction is noticeable in these instances.

Dilatation, and not constriction, occurred in the case of the coronary (Fig. 5) and cerebral arteries, the reaction in the cerebral being, however, extremely slight. This dilatation was abrupt in onset after a very short latent period, the maximum was quickly reached, and the vessel preserved its condition of diminished tonus for a considerable time.

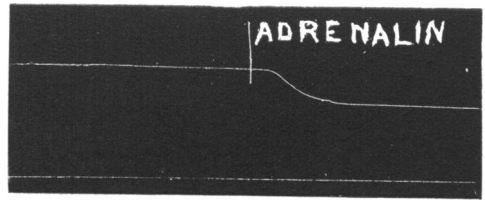

Fig. 5. Ring preparation of sheep's coronary artery.
Shows the effect of adrenalin.

The results of these experiments agree very closely with the results of previous observers, the only difference being in the case of the coronary artery. Whereas Schäfer concluded that the increase of flow in the coronary arteries, which he noted as taking place when the heart was perfused with adrenalin, was due to increased activity of the heart-muscle, I have shown that adrenalin causes an active dilatation of the coronary artery.

Adrenalin then has a very marked power of constricting the arteries, with the exception of the intravisceral portion of the pulmonary artery, the coronary and the cerebral arteries; and that in the two last adrenalin causes dilatation.

The following table shows in a graphic manner the degree of reaction of the various arteries to adrenalin:

1.	Splanchnic arteries	very marked constriction.
2.	Carotid artery and branches	marked constriction.
3.	Arteries of lower extremity	moderate constriction.
4.	Pulmonary artery (extravisceral) ...	moderate constriction.
5.	Intercostal artery	slight constriction.
6.	Pulmonary artery (intravisceral) ...	no reaction.
7.	Cerebral artery	slight dilatation.
8.	Coronary artery	moderate dilatation.

It may be argued, then, that although there are no vaso-constrictor nerve-endings in the coronary arteries, they do contain vaso-dilator nerve-endings; and the same remark applies to the cerebral arteries: and again that whereas the pulmonary artery in that portion which is outside the lung is innervated, the intravisceral portion is devoid of vaso-motor innervation.

Barium chloride was employed as a typical muscle stimulant. Twenty-five experiments were performed. In every case the artery reacted by constriction. The reaction was most marked in the case of

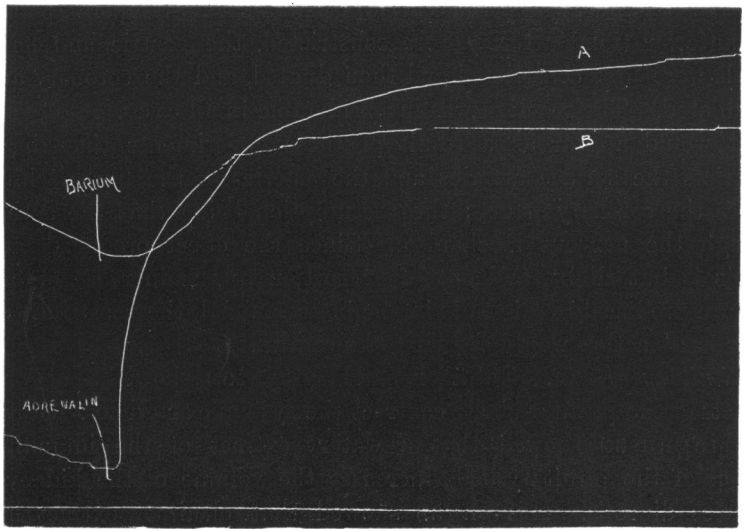

Fig. 6. Ring preparation of sheep's pulmonary artery. Main stem. Showing the relative effect of barium and adrenalin. When the drugs were applied the vessel was still relaxing as a result of a rise in temperature.

the gastric, hepatic, splenic and renal arteries; the other arteries showed a progressively diminishing reaction in the order in which they are named: carotid and its branches, pulmonary, popliteal and anterior tibial, coronary, cerebral and intercostal. In the case of the two last mentioned vessels constriction was extremely small.

A distinct difference was noticed in the character of the constriction produced by barium and adrenalin (Fig. 6). In the case of adrenalin the constriction was marked and rapid in onset, the maximum was soon reached, and the vessel remained in a state of increased tonus for some time; whilst in the case of the reaction to barium the constriction was less rapid in onset and of rather smaller amount, the maximum was not reached for a considerable time, and when reached the condition of increased tonus was not preserved for so long a time as after the administration of adrenalin.

One may conclude that barium constricts all vessels that contain an appreciable amount of muscle tissue, and that its effect is roughly proportional to the amount of muscle present in the vessel wall.

Digitalis. I performed 12 experiments with this drug. In order to eliminate any possible error due to the action of alcohol in using a preparation such as the tincture of digitalis, a watery solution of the drug was used[1]. It was found that different arteries reacted differently to the drug; thus, whilst the carotid, facial, auriculo-temporal, popliteal and anterior tibial arteries were constricted, the gastric and hepatic vessels were first constricted and then dilated, and the coronary artery was dilated. The reaction was inconsiderable in all cases.

It would appear as a result of these experiments that digitalis constricts the surface arteries and the arteries of the limbs, whilst it dilates the coronary artery; the presumption being that the action is through the nervous mechanism. Since the effect produced on the vessels is but slight, and out of proportion to the increase of blood-pressure produced by digitalis in the intact animal, the most important factor in its action would appear to be central.

Pituitary extract. Schäfer and Vincent(15) showed that watery extracts of the pituitary body contract the systemic arterioles. Schäfer and Magnus(16) showed that a watery extract of the infundibular portion of the pituitary body increases the volume of the kidney and produces diuresis. Herring(17) showed that pituitary extract has a selective action on the kidney, producing dilatation of the renal blood vessels. He(18) concluded that pituitary extract acts by stimulating

[1] Digitalone (Parke Davis & Co.).

vaso-motor nerves. Pal(19) also working with Meyer's method showed that pituitary extract acted on the carotid, mesenteric and femoral arteries in the same way as adrenalin, but on the coronary and peripheral end of renal its action was opposed to that of adrenalin.

Thirty-six experiments were performed, the results of which varied according to the artery which was being used. With the carotid and its branches constriction was produced; with the intercostal, cerebral and pulmonary arteries no appreciable effect was produced; with the coronary artery an indefinite result was obtained, sometimes constriction and sometimes dilatation. The gastric and renal arteries were dilated, whilst at first it appeared that the splenic and hepatic vessels might be dilated or constricted.

As the results obtained were so unequal, I performed an extended series of experiments with the splanchnic vessels, using at first different doses of the drug in different experiments. I found, however, that no variation in the dose instilled, from 0·1 c.c. to 1 c.c., produced any change in the character of the response, which in all cases was a constriction.

I then tried the effect of using different balancing weights on the recording lever in different experiments, weights of one, two and four grms. being tried. Here again, however, the results were uniform, the artery responding in all cases by constriction.

I next tried the experiment of taking rings from different portions of these arteries, and comparing their reactions to the drug, and here I found the cause of the apparently inexplicable fact that the same artery had at different times given diametrically opposite reactions to the same drug. I found that rings taken from the hepatic, splenic and gastric arteries in the neighbourhood of their origin from the cœliac axis might react either by constriction, or by a scarcely perceptible dilatation; whereas rings taken from the visceral ends of these arteries reacted in every case by a more marked dilatation, and this in spite of the fact that the diameter of the artery is naturally smaller at the distal than at the proximal end. Rings taken from portions of these arteries between the proximal and distal ends were found to react by dilatation, which dilatation became more and more marked the nearer the part from which the ring was taken approached the respective viscus. Similarly, in the case of the renal artery I found that, whilst on no occasion was I able to demonstrate a constricting reaction with any part of the artery, the dilatation became progressively more marked the nearer the part of the artery, from which the ring was taken,

approached the kidney. Fig. 7, taken from one of these experiments, illustrates this.

The reactions produced by pituitary extract, whether of constriction or dilatation, are in no case so abrupt in onset as those produced by adrenalin. With pituitary extract as the stimulant it is a rare occurrence for the writing lever to describe a tracing the direction of which at any part exceeds an angle of 45° with the horizontal; whereas with adrenalin an angle of 90° was frequently approached.

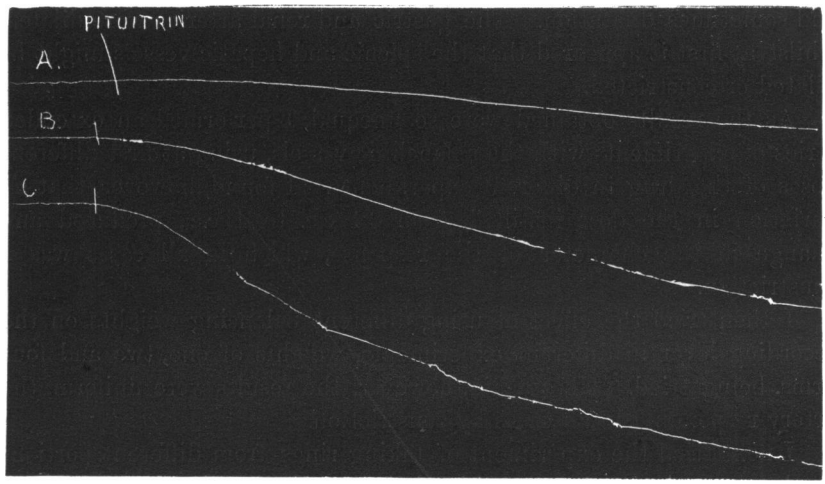

Fig. 7. Ring preparations of sheep's gastric artery. Showing the effect of pituitrin at the indicated marks. *A*, near the cœliac axis, *B*, two inches lower, *C*, near the pylorus. The coefficients of these are respectively 12, 33, 47.

The degree of dilatation produced by pituitary extract is considerably greater than the degree of constriction produced, which latter never approached the degree of constriction produced by adrenalin.

The condition of increased tonus produced by pituitary extract was not maintained for long; the maximum was not reached for a considerable time after the constriction had begun; and, when reached, the tonus soon started to relax again. In no case was the duration of increased tonus comparable to that produced by adrenalin.

As a result of these experiments it would appear that the conclusions of previous observers are in the main confirmed; also that the splanchnic vessels have a peculiar vaso-motor mechanism, which enables them in one part to constrict and in another part to dilate at the same time to the same drug.

Since pituitary extract causes a general increase of blood-pressure in the intact animal, it follows that, *cæteris paribus*, the constricting effect on the systemic vessels generally must outweigh the dilating effect on the splanchnic vessels; or else we must believe that pituitary extract has, besides a peripheral action, a central action, which possibly tends to hold in check the local dilating effect on the splanchnic arteries.

If it is the case, as Houghton and Merrill(20) showed, that the increase in blood-pressure, produced by pituitary extract in the intact animal, is of longer duration than that produced by adrenalin, we must conclude that, apart from its direct action upon the vessels, which I have shown to be of shorter duration than that produced by adrenalin, there is a central action also, which is more lasting than the peripheral effect, or what appears even more probable that pituitary extract contains a dilator and constrictor substance.

Ergot, ergotoxin, tyramine and isoamylamine. Dale and Dixon(21) and others have shown that certain amine bodies, produced by putrefactive action, have an action similar to that of adrenalin; it has also been shown that certain of these bodies are present in watery extracts of ergot, and that they are responsible for almost the whole of the pressor action of the liquid extract.

I performed 17 experiments with these drugs. The results were constant in showing that a considerable degree of constriction is produced in all cases with but one exception, the pulmonary artery, on which no effect was produced. As regards the character of the constriction produced, that caused by ergotoxin was of considerably longer duration than that caused by either the liquid extract of ergot, tyramine or isoamylamine. The constriction produced was at the best moderate in amount, and of short duration.

It may be concluded from the results of these experiments that, since the intravisceral pulmonary artery, which has no vaso-constrictor nerve-endings, is the only artery unaffected by these drugs, these drugs produce constriction by stimulating nerve-endings.

Sodium nitrite and amyl nitrite. It has been known for many years that the nitrites produce vaso-dilatation. Brunton(22), as long ago as 1870, concluded that the lowering of blood-pressure, caused by amyl nitrite, is due not to weakening of the heart's action, but to a dilatation of the vessels, and that this dilatation is due to the direct action of the drug upon the vessel walls.

Twelve experiments were performed—the arteries responding by dilatation in all cases. The dilatation produced by sodium nitrite was generally speaking more marked than that produced by amyl nitrite; this drug, however, could not be brought to act on the ring of artery in the same way as the former on account of the difficulty of solution. The dilatation produced was in most cases abrupt in character, the maximum degree of dilatation was soon attained, and the vessels remained dilated for a considerable time. The fact that dilatation was produced in the case of all the vessels, coronary and pulmonary as well as systemic, argues that the action is one on the muscle tissue of the vessel-wall and not on the nerve-endings.

Calcium chloride. Hans Meyer(23) showed that the administration of calcium salts inhibits inflammatory exudation, and that withdrawal of the normal calcium salts produces a hyper-irritability of the sympathetic system towards adrenalin and other drugs.

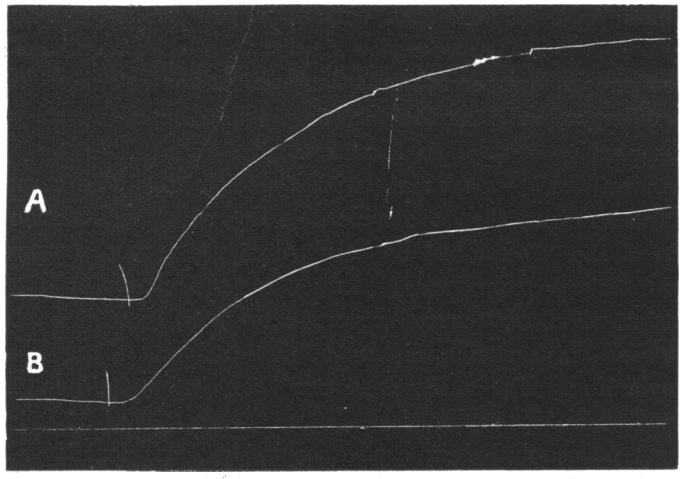

Fig. 8. Ring preparations of sheep's splenic artery. Showing the effect of adrenalin in *A*, calcium-free Ringer, and *B*, in Ringer's solution containing a slight excess of calcium chloride.

Eight experiments were performed. It was found that when the arterial ring was placed in calcium-free saline solution, and adrenalin and pituitrin instilled, a greater reaction occurred than followed similar doses of these drugs when the experiment was performed in saline solution containing an excess of calcium salts (Fig. 8). As might be

expected, far smaller differences were to be noted in the reactions when the experiments were performed in normal saline solution (containing ·2 gram of calcium chloride in 1 litre) than in saline solution containing an excess of calcium salts.

The reactions due to barium chloride showed no appreciable difference, no matter in what proportion calcium salts were present.

Sparteine. This alkaloid has been recommended as a cardiac and muscular tonic, which was supposed to exert an action similar to that of digitalis on the heart and blood vessels(24). It has been pointed out recently that this is not the case; but that sparteine is a depressant, lowering the blood-pressure by a dilatation of the peripheral vessels.

I performed five experiments with this drug, the vessels used being the carotid, gastric and anterior tibial. Each of these arteries responded by decided dilatation.

Caffeine, urea and sodium sulphate. The effect of these three drugs, each having a marked diuretic action, was compared on the renal artery with some other systemic artery.

A series of nine experiments was performed with the object of demonstrating whether any or all of these drugs had a specific dilating effect on the renal artery. It was found that caffeine, whilst moderately dilating the renal artery, produced an equal amount of dilatation in the case of the splenic artery, and had no appreciable effect on the carotid artery.

Urea was found to produce more dilatation in the case of the splenic than in the case of the renal artery, the carotid artery being unaffected.

Sodium sulphate produced a scarcely appreciable dilatation of the carotid artery, a more marked dilatation of the splenic artery, and a still more marked dilatation of the renal artery; though in none of these cases was the resulting dilatation of any considerable amount.

These experiments show that the drugs under discussion exert a more pronounced vaso-dilatation on the splanchnic vessels than on other systemic vessels; but no significant difference could be determined between the renal and other splanchnic vessels.

In order to bring out more clearly the comparative effects of the more important vaso-motor stimulants on different arteries, I have worked out a series of coefficients, which roughly represent the degree of constriction or dilatation produced by different reagents on different arteries.

The formula employed is as follows:

$$\text{Coefficient} = \frac{x \times 100}{y} \times \frac{6}{145}, \text{ when}$$

x = the difference in height of tracing above base-line, before and after the application of the stimulant; expressed in millimetres.

y = the long diameter of the flattened artery; expressed in millimetres: the length of the short and long arms of the recording lever being 6 and 145 millimetres respectively.

I give the coefficients thus obtained in tabular form:

	Temperature	Adrenalin	Barium	Pituitrin
Carotid artery	−31	+27	+17	+1
Facial artery		+43	+33	+5
Auriculo-temporal artery		+10	+ 4	
Intercostal artery	− 8	+ 8		
Anterior tibial artery		+16	+ 5	
Pulmonary artery		+40	+33	
Coronary artery	−10	− 9	+ 1	+ } 4
Cerebral artery	− 8	− 3	+ 3	− }
Gastric artery	−78	+68	+25	−40
Hepatic artery	−46	+38	+29	−46
Splenic artery		+47	+33	−54
Renal artery	−43	+43	+11	−32

It will be seen from the above table that the greatest coefficient for each artery is obtained by variation of temperature, and that this coefficient is very nearly approached in most cases by that of either adrenalin or pituitrin. It will also be noticed that in the case of the splanchnic vessels the coefficient of pituitrin is very much higher than in the case of the other systemic vessels—in other words, that as far as local action on the arteries is concerned, pituitrin has a far more powerful action on those arteries which it dilates than on those which it constricts; and in consequence, unless pituitrin has some central action, one would expect that its administration to the intact animal would be followed by a lowering and not an increase of blood-pressure.

I give here a second table of coefficients, to emphasize the graduated response of certain arteries to adrenalin and pituitary extract.

Pulmonary artery:

	Main stem	Primary branch outside lung	Branch at root of lung	Branch within lung
Adrenalin	+42	+35	+18	0

Gastric artery:

	Near origin	2″ lower	Near pylorus
Pituitary extract	−12	−33	−47

Splenic artery:

	Near origin	Near spleen
Pituitary extract	−6	−33

Hepatic artery.

	Near origin	2″ lower	Near liver
Pituitary extract	+12	−17	−18

Renal artery:

	Near origin	Near kidney	Within kidney
Pituitary extract	−13	−30	−30

In a few of my experiments I have been surprised by a peculiar action shown by the artery when contracting and in states of increased tonus. In these, instead of responding in the ordinary way and recording its contraction by a tracing line of more or less uniform direction, the upward movement of the writing lever was broken up into a series of rhythmical contractions and relaxations, so that whilst the main direction of the writing lever was upwards, the tracing gave a remarkable wavy appearance. A specimen of this variation is shown in Fig. 9. Two doses of ergot had been applied, followed by a single

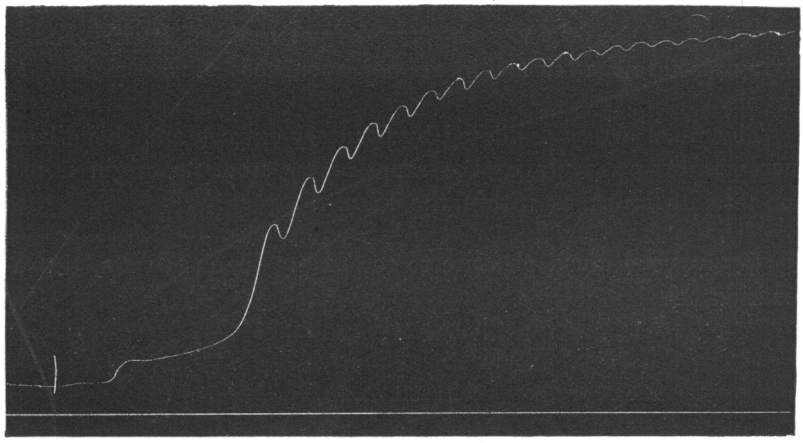

Fig. 9. Ring preparation of sheep's gastric artery, showing the effect of adrenalin in producing rhythmical contractions.

dose of adrenalin, which provoked the artery into responding in the manner shown. On analysing this tracing it is found that the average time occupied by one of these rhythmical units is 25 seconds. The average duration of the Traube-Hering curve corresponds to eight respirations, or roughly speaking 30 seconds. Is this rhythmical contraction of the arteries the cause of the Traube-Hering curve, which has always been supposed to be due to central action? At all events it is

evident that under certain conditions the arteries have the power of producing intrinsic rhythmical contractions.

From the foregoing results it would appear that certain arteries have certain peculiarities in their reactions to various stimulating agents.

Briefly summarised, the coronary artery, and, to a smaller extent, the cerebral artery are dilated by adrenalin; whereas this drug produces constriction on all other arteries.

The pulmonary artery may be divided into two portions, that without the lung, which reacts to adrenalin in the same way as other arteries, and that within the lung, which either is not affected by adrenalin, as my experiments would tend to show, or is actually dilated, as shown by Brodie and Dixon. Furthermore, the pulmonary artery reacts to adrenalin in a progressively diminishing degree the nearer the part of the artery in question approaches the lung.

The gastric, hepatic and splenic arteries are generally speaking dilated by pituitary extract, this dilatation decreasing progressively from the viscus to the origin of the vessel from the cœliac axis, and even giving place to constriction in the neighbourhood of the origin of these vessels.

The renal artery is dilated by pituitary extract, and this dilatation increases progressively in the same artery from its origin from the aorta to its branches within the kidney.

It gives me much pleasure to record my thanks to Dr Dixon for his kind help and advice.

REFERENCES.

(1) MacWilliam. Proc. Roy. Soc. LXX. p. 109. 1902.
(2) Meigs. Amer. Journ. of Physiol. XXIV. p. 1. 1909.
(3) Barcroft and Dixon. Amer. Journ. of Physiol. XXXV. p. 182. 1907.
(4) Dixon. Amer. Journ. of Physiol. XXXV. p. 346. 1907.
(5) Kobert. Arch. f. exp. Path. u. Pharm. XXII. p. 90.
(6) Schäfer and Oliver. Journ. of Physiol. XVIII. p. 230.
(7) Brodie and Dixon. Journ. of Physiol. XXX. p. 476.
(8) Plumier. Journ. de Physiol. et de Path. VI. p. 655. 1904.
(9) Wiggers. Journ. Pharm. and Exp. Therapeutics, I. p. 341. 1909.
(10) Langley. Journ. of Physiol. XXVII. p. 237.
(11) Schäfer. Impr. de l'Inst. Imp. de Méd. Exp. Dec. 1904.
(12) Wiggers. Amer. Journ. Physiol. XX. p. 206. 1907–8; XIV. p. 452. 1905. XXIV. p. 391. 1909.

(13) Dixon and Halliburton. Quart. Journ. of exp. Physiol. III. p. 4. 1910.
(14) Langley. Journ. of Physiol. XXXII. 1905.
(15) Schäfer and Vincent. Journ. of Physiol. XXV.
(16) Schäfer and Magnus. Journ. of Physiol. XXVII.
(17) Herring. Quart. Journ. of exp. Physiol. I. p. 2. 1908.
(18) Herring. Journ. of Physiol. XXXI. p. 429.
(19) Pal. Wiener klin. Wochensch. Nr. 51. 1908.
(20) Houghton and Merrill. Journ. American Med. Assoc. Nov. 28, 1908.
(21) Dale and Dixon. Journ. of Physiol. XXXIX. p. 25.
(22) Brunton. Journ. of Anat. and Physiol. V. p. 92.
(23) Hans Meyer. Brit. Med. Journ. 19. XI. 1910.
(24) Cushny and Matthews. Arch. f. exp. Path. u. Pharm. XXXV. p. 129.