

Harvey Lecture.

VASOMOTOR RELATIONS.*

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THE invitation to address this distinguished audience is especially welcome, because we who are thus honored are given the unusual privilege of speaking more or less informally. This is as it should be. In the conventional lecture, truth is dragged from a warehouse, imperfectly dusted and set before us. We are untouched. Which of us rises when gravitation is mentioned and stands with reverent head before that awful phenomenon? But discoveries in the making have strange power — an amazing, embryonic energy; they trouble yet charm the mind. The glow of the forge and the sound of beaten iron will stir our sluggish souls. To the investigator there is no greater pleasure, saving that of his work itself, than to go with others to the edge of the darkness and point the direction in which he thinks the next light will appear.

At the beginning of any extended study of a physiological theme, it is well to take a general view, with an eye to determining whether the means are justly proportioned to the desired end. We desire, no doubt, that vasomotor relations in man and in other animals shall be fully understood. At once there arises the difficulty that experimentation on man is properly very limited. Human conditions make it usually impossible to subdivide a general problem like the vasomotor relations into those simple constituents which alone can be made the subject of exact experimentation. This great difficulty is not sufficiently appreciated, especially by practitioners. To secure the necessary factorial simplicity, the investigator must inevitably choose the higher animals for all or almost all the exact measurements that he requires. The measurements made on any one species, for example, the rabbit, will primarily be useful as regards that particular animal, but it does not follow that they will be applicable to man and other animals. To apply to man the blood pressure data obtained from the rabbit or from any other species, it must first be shown that the phenomena in question are quantitatively the same in all the higher animals, or at least the limits of variation must be quantitatively determined. It will then be possible to fix the degree of probability that man will follow the law proved true for other mammals. These basal conditions are so evident that the lack of quantitative measurements of vasomotor phenomena from the comparative standpoint must excite surprise. It is known, for example, that the stimulation of nerves afferent to the vasomotor centre is an important factor in the regulation of the blood pressure. A rise in blood pressure has been shown to

follow such stimulation in many animals, but the quantitative relations have never been studied.

The writer and Mr. Russell Richardson have therefore measured the rise in blood pressure produced by stimuli of the same intensity applied to the sciatic and the brachial nerves of the rabbit, cat, dog, guinea pig, rat and hen. A mercury manometer was connected with the carotid artery or, in the case of the hen, with the femoral artery. Just enough curare to prevent muscular reflexes was injected through a vein.¹ The nerves were then stimulated with induction currents of uniform intensity, and the consequent rise in blood pressure recorded with the kymograph. The figures thus obtained gave the absolute change in blood pressure upon stimulation of an afferent nerve.

At this point, it was necessary to adopt the principle of percentile values. The absolute change in blood pressure obtained at one level cannot be compared directly with that obtained at a different level. For example, in one series the stimulation of the sciatic nerve in the rabbit, while the blood pressure was 100 mm. Hg, caused a rise of 35 mm., and when the blood pressure was 50 mm., a stimulus of equal intensity still caused a rise of 35 mm. The absolute change was the same in both, but in the first instance this change was 35%, while in the second it was 70%. This is the well-known difference between the moral and the statistical value.² An unfaithful trustee robs two women. One of these has \$40,000, the other \$20,000. From each he takes \$10,000. Their absolute loss is the same, but one woman can still live on her income, while the other must work or beg. It is necessary, then, in measuring vasomotor reflexes to take into account the level of the blood pressure at the beginning of stimulation, and this is done by expressing the change in blood pressure as a percentage of this level.

To the percentile values obtained in the investigation of which we speak were added 796 records of brachial stimulation and 248 records of sciatic stimulation obtained from the rabbit, cat and dog in previous investigations.³ The percentile changes were averaged in each animal. These averages are at present as follows:⁴

	Sciatic.	Brachial.
Rabbit,	56	47
Cat,	47	45
Dog,	25	30
Guinea pig,	34	33
Rat,	55	41
Hen,	54	41

The figures permit the gratifying conclusion that, on the whole, the vasomotor relations in these animals are fundamentally alike.

Important consequences flow from this new fact. The functions of living tissues may be divided into two groups, which may be termed fundamental and accessory. The respiration and the maintenance of body temperature, reproduction, are fundamental; the representation of skilled movements in the cortex is accessory. Existence depends on the first group, civilization on the

* This Harvey lecture was delivered without notes, and was over an hour in length. Considerations of space make it desirable to omit from the present report all data that have not fallen recently under the writer's own observation. Some of the researches mentioned in the lecture as delivered have since been considerably advanced. The additional facts are included in this paper.

second. In which class does the maintenance of blood pressure fall?

It is characteristic of the fundamental phenomena that they are little disturbed by afferent impulses. They are of ancient origin; for eons they have practised against the swarms of stimuli that strike upon the periphery. Were our ears more sensitive, we should hear these stimuli as we hear the drum of rain upon the roof. Yet the fundamental functions take their way unvexed. The respiratory rhythm goes on almost without change and the balance between heat production and heat loss is maintained in spite of all vicissitudes.

What I have termed the accessory functions, on the contrary, are comparatively recent. They have not the poise of countless generations, nor can they so readily defend themselves against the afferent stream, which now rises against them as Scamander rose against Achilles. In the beginning, men watched their flocks upon the hills or dug their fields. The irritability of the peripheral organs was sufficient for the day and the evils thereof. In the slow lapse of time afferent and efferent impulses grew up in equilibrium, side by side. Man and the higher animals moved calmly in a simple environment. Compared with the ages that have gone in the attainment of this equilibrium, civilization is of yesterday. Our environment is suddenly changed. Stimuli in our urban life have increased until they drive against us like a storm. At the same moment, our peripheral irritability has been enlarged by the habitual use of newly discovered poisons, by housing skins made for the open air, and by many another device of those who dwell in towns. Much depends, therefore, on whether the blood pressure shall be reckoned with functions that are resistant to afferent impulses or with those that are easily their prey.

The research we are discussing answers this question with at least a considerable measure of probability. It is unlikely that animals so diverse as those here stimulated would give quantitatively so nearly the same response were not the maintenance of blood pressure like the maintenance of body heat, a fundamental phenomenon developed to the same high efficiency in many, perhaps in all warm-blooded animals. This conclusion is supported by the investigations next to be considered. Impulses of moderate intensity are the portion of the fortunate. In surgical injury or disease, we must believe, the cells whose function it is to safeguard the general blood pressure are beaten upon by violent afferent streams.⁵ These ordeals are infrequent; in the usual or normal life they may not occur at all. How do the vasomotor cells support these sudden strains? Are they overwhelmed by a summation of extraordinary impulses, or is the margin of strength great enough to meet an emergency so rare that prevision would seem almost wasteful?

This problem has been attacked in two ways. First, by the injury of regions, such as the cerebral hemispheres and the abdominal viscera, known to be richly connected with the vasomotor cells, and

secondly, by the direct stimulation of nerve trunks known to contain fibers afferent to those cells.

The injuries to the brain were as follows: 1. Concussion, often with fracture and intracranial hemorrhage, from blows on the head of the etherized animal. 2. Penetrating wounds, produced by driving a pointed instrument into the brain. 3. Removal of brain substance. 4. Increased intracranial pressure. The animals employed were rabbits and cats. The blood pressure was recorded by a membrane manometer, which was frequently calibrated with a mercury column. Afferent impulses were obtained by the electrical stimulation of the central end of the depressor, sciatic, and branches of the brachial nerves in or near the axilla. Precautions were taken to have the curarization uniform. Among the injuries was fracture of the base of the skull with hemorrhage through the external ear. In two experiments, the cerebral hemispheres were completely removed.

In none of the experiments was the change in blood pressure on stimulation of the afferent nerve diminished; on the contrary it was increased. In the experiment of March 13, 1905, for example, the stimulation of the sciatic nerve in the as yet normal animal caused a rise of 28%, but after the removal of the cerebral hemispheres, a stimulus of equal intensity caused a rise of 47%.

Injuries of the abdominal viscera were studied in 1903,⁶ and subsequently the normal fall of blood pressure produced by stimuli of uniform intensity applied to the central end of the depressor nerve was measured in the rabbit and the cat. The intestines were then painted with nitric acid or otherwise treated to produce a great fall in blood pressure together with the other clinical signs of shock. After many hours, the stimulation of the afferent nerve was repeated. It was found that the percentile fall obtained during shock was little if any less than that obtained before shock appeared.

The following is an example:

At 9.30 A. M., the intestines of a rabbit were painted with nitric acid. The stimulation of the depressor nerve caused the blood pressure to fall from 67 to 36 mm. (46%). Eight hours later, the rectal temperature was 26°, and the blood pressure was about 35 mm. The stimulation of the depressor nerve still caused the pressure to fall about 40%.

Burning the skin and crushing the testis were also without effect in producing a significant fall in blood pressure. Thus on Nov. 12, 1906, in an etherized dog, the prolonged stimulation of the testes with weak and strong tetanizing currents did not lower the carotid blood pressure, nor did repeated crushing of the testes half an hour later.

Since these experiments were first made, the writer has performed many similar operations in which the results confirm in all respects the conclusion that the vasomotor cells retain their irritability in spite of the extensive injury of peripheral organs and tissues.

The second method of attacking this question was by the stimulation of nerve trunks containing

fibers afferent to the vasomotor cells.⁷ The central ends of the divided sciatic nerve, the brachial nerves, the posterior spinal nerves, were stimulated. The following are examples:

Experiment, July 10, 1905. — A cannula was placed as usual in the carotid artery of a cat anesthetized with ether. There was a considerable loss of blood through a defective seam in the rubber cannula-tube. The posterior root of the fourth lumbar nerve was stimulated three hours. The rate was eleven induction currents per ten seconds. In spite of the prolonged stimulation following the hemorrhage noted above, and the severe operation upon the spinal cord, the blood pressure fell no more than in a control animal subjected to the same manipulations, except the hemorrhage and the stimulation of the nerves.

Experiment, Nov. 12, 1906. — In an etherized dog, the brachial and sciatic nerves were stimulated with strong tetanizing currents at intervals for two hours and forty minutes, but no significant fall of blood pressure was observed.

Experiment, Sept. 6, 1907. — The large hemispheres of an etherized cat were divided transversely above the pons by a blunt seeker introduced through a small trephine hole. The ether was then discontinued. At intervals of one or two minutes, strong currents from the inductorium were passed through the central end of the sciatic nerve for thirty seconds. This continued from 11.30 A.M. to 1.30 P.M. At the beginning the blood pressure was 80 mm.; on stimulation of the sciatic, it rose to 105 mm.; two hours later, the blood pressure was 60 and rose to 113 mm. on stimulation.

The numerous stimulations made in this investigation uniformly failed to give a significant fall in blood pressure.

Thus neither afferent impulses developed by the injury of important peripheral regions, nor the impulses produced by the stimulation of afferent nerve trunks are able to cause more than a momentary change in that general blood pressure upon the preservation of which the vital functions depend. Apparently, there is an excess of strength, a prevision that is wasteful, since the fate against which it is created does not enter the ordinary life.

A more satisfactory explanation of this remarkable protective mechanism is probably to be found in an observation recently made by the writer and Mr. Richardson. It is known that skeletal muscles do not contract when very weak electrical currents are passed through them. As the stimuli are increased in intensity, a point called the "threshold value" is reached at which the stimulus is just sufficient to call forth a feeble contraction. With a continued increase in the stimulus, there is a continued increase in the contraction, until, at length, the maximum shortening is obtained. The muscle has now done its best and no additional stimulation, however powerful, will call forth any further shortening. The normal heart muscle, on the other hand, will give its maximum contraction to any stimulus that will make it contract at all. The writer wished to determine whether the vasomotor cells were discharged after

the manner of the skeletal or the cardiac muscle. The vasomotor nerves keep the gates through which the blood flows to the tissues. Thus the renal nerves modify the amount that shall pass the secreting cells of the kidney and the rate at which this blood shall move. The problem was whether the gate opened wider to a strong afferent impulse than to a weak one, or whether any adequate stimulus, *i. e.*, any stimulus beyond the threshold value, would at once open the gate to its full extent. Experimentation shows that the former is the case.⁸ A wide interval separates the threshold from the maximal reflex rise in blood pressure obtained by stimulating the central end of the sciatic or brachial nerves. The maximal value, however, is unmistakably marked. It is this maximal value that protects the vasomotor apparatus against excessive stimulation.

With this investigation are connected others of much interest. Studies are being made to determine whether the several neurons which make up the vasomotor chain have an equal share in this protective action. It is possible that the brunt of it falls on the muscle of the arterial walls.

We are measuring also the relation between the number of afferent fibers stimulated and the resultant discharge of the vasomotor center. Does the same stimulus applied to many afferent fibers discharge the vasomotor reflex more easily or to a greater extent than when applied to only a few afferent fibres? Upon this must often depend the relation between the size of a stimulated area and the effect of its stimulation upon the distribution of the blood. The bearing of this investigation upon the theory of counterirritants and the mechanism by which surface injuries produce their effects is evident.

Further information regarding these interesting problems is afforded by another investigation, also under way. It is known that cold applied to one portion of the surface of the body may congest a distant region, while the same stimulus applied elsewhere on the surface will fail to do this. The vasomotor system is rich in association paths, creating a community of interest in certain reflexes. Our knowledge of these associations should be increased by systematic exploration, quantitative where possible. We are therefore measuring vasomotor reflexes, nerve by nerve.

With these same studies is combined an inquiry into a different sort of relation between afferent fibers and the vasomotor center. We are not yet certain whether the vasomotor cells are automatic or whether they would be unable to preserve the vasomotor tone without the aid of afferent impulses. These cells may either originate the impulses that keep the vessels constricted, or they may serve simply as transformers of the impulses that are brought to them. The same doubt exists with regard to the reflex or automatic nature of the respiratory center.

It is known, chiefly through the researches of Marcwald, that although great numbers of afferent nerves will superficially modify the respiration, there are some which are especially related to the respiratory center. Thus the separation of

the pons from the bulb, followed by the section of the vagi, will completely alter the respiratory type, and the normal rhythmic respiration will give place to spasmodic respiratory movements of remarkable extent. It is important that we should know whether there are afferent nerves that possess a similar relation to the vasomotor center.

But let us turn from observations about to be made to those already secured. In the course of the investigation into the vasomotor reflexes of different classes of animals, it was noted that the normal blood pressure stood at somewhat different levels in different animals. These levels do not agree very closely with the few measurements already recorded in the literature, but that is another question. At present, let us consider the probable analogy between the balance or equilibrium reaction, which we call the blood pressure, and the balance reaction known as nitrogenous equilibrium. Nitrogenous equilibrium may be obtained at different levels. Indeed, it is now a burning question whether scholars should eat much or little proteid. Certainly, nitrogenous equilibrium should vary with the work to be done, just as the ratio of proteid to carbohydrate in the diet of the dairy cow is made to vary with the quantity of milk produced. So also should the vasomotor status vary. The protection afforded by a strong vasomotor tone is not essential to the indoor life and indeed may be disadvantageous as it throws increased work upon the heart. On the other hand, house-bound persons are exposed to dangerous congestions when they carelessly take their low-toned vascular areas out of doors. The maladjustment between afferent and efferent impulses is the source of many ills in our modern life. Who does not know the unhappy person of low vasomotor tone who falls asleep upright in his chair and, being admonished, goes to bed only to find himself wide awake as soon as he lies down. The congestive headache, and even the beginning arteriosclerosis, can be conquered by patient study in this field.

In the research upon the effect of uniform afferent impulses upon the blood pressure at different levels,⁹ the writer determined that the absolute change in blood pressure on stimulation of afferent nerves was about the same so long as the blood pressure at the beginning of stimulation was not less than about 55 mm. Hg. Below that point, the absolute change slowly diminished. Above 55 the reflex was independent of the initial blood pressure, but below 55 the reflex lessened at a rate parallel to the diminution in the initial blood pressure.

The relative or percentile change in blood pressure, which is the true index of the condition of the vasomotor cells, increases as the blood pressure falls. In the case of the sciatic nerve this increase persists until the blood pressure is about 30 mm. In the case of the brachial nerve, the increase lessens when the blood pressure has fallen to about 65 mm. Hg,¹⁰ but with both the brachial and the sciatic nerves the percentile rise is greater even when the blood pressure has fallen to about

30 mm. Hg, which is the blood pressure after destruction of the spinal cord, than at the normal level of about 150 mm. Hg. Thus, as the blood pressure falls, the power of the brachial and sciatic fibers increases. The brachial and sciatic nerves here display a protective action. The same stimulus produces relatively a larger increase in the blood pressure as the danger of bulbar and spinal anemia grows. The greater the danger, the greater the reflex.

The investigation regarding the interval between the minimum and maximum value for reflex stimulation has already been mentioned. It will be interesting to determine whether this interval remains unchanged in spite of changes in the level of the blood pressure before stimulation.

It is sometimes asserted that hemorrhage may enable a previously inadequate stimulus to lower the blood pressure even in dangerous degree. A special research¹¹ has been undertaken, with Mr. H. K. Marks to determine this question. The material, so far as analyzed, does not support the view just mentioned. The stimulation of afferent nerves still produces the familiar rise in blood pressure even when the hemorrhage has reduced the initial blood pressure to a very low level. This question and the allied problem how far anemia of the bulbar vasomotor cells modifies the reflex, the writer expressly reserves for the investigation upon which progress was reported at the meeting of the American Physiological Society in December, 1906. The method employed is the feeding of the brain by an independent circulation, under the control of the operator. Local variations in the circulation of the bulb are thus made possible while, at the same time, the general circulation serves to measure the vasomotor reflexes discharged by the isolated bulb.

There has been of late renewed discussion as to the cause of the symptom-complex termed shock. Concerning the symptoms themselves, there is very general agreement, — they are indeed but too well known to every surgeon, — the abnormal fall of blood pressure, the failing heart, the low temperature, the apparent depression of the nervous system are frequent tokens of calamity. It is the apparent depression of the nervous system that has for many years given such favor to the idea that the low blood pressure is the result of exhaustion of the vasomotor center. Men forget that the brain is not an organ, but a region, very large in proportion to the groups of nerve cells that are scattered through it like settlements in a wilderness of fibers. It is forgotten, too, that these cell groups have the most diverse functions. Thus, as in the writer's experiments, the large hemispheres may be roughly taken away without lowering the normal blood pressure and without affecting the vasomotor reflexes, except to increase them. The depression observed in shock does not therefore justify any sweeping statements regarding the condition of the many separate nerve-organs sheltered by the cranium and the vertebral canal. Rather, should the condition of each group of nerve cells be tested by trust-

worthy methods. It was with this end in view, no doubt, that experiments have recently been made in this country on shock produced chiefly in dogs. These experiments have led to the statements that the reflex rise of blood pressure on excitation of the central end of the sciatic nerve is diminished during shock and that it fails altogether in the graver stages. These statements are partly correct, but by a common paradox their partial truth makes them wholly misleading. It has been shown above that the blood pressure may fall from 150 to about 50 mm. Hg, and even the absolute rise on stimulation of the sciatic nerve remain unchanged. The fall in blood pressure is the most significant symptom of shock. Opinion as to the extent to which the blood pressure must fall to bring the case within the category of shock can be gained by taking the average of the observations made by some clinician who has experimented on this subject. In the first fifty pages of a recent treatise¹² are recorded 28 experiments on dogs, in which the blood pressure at the beginning of the experiment averaged 132 mm., while the blood pressure after shock was present, averaged 57 mm. Hg.¹³ It is evident that in the present writer's experiments the absolute reflex rise was maintained even after the initial blood pressure had sunk to a level usually taken to be symptomatic of shock. But the absolute rise is of little critical value. For reasons already set forth, it is the percentile rise that is the just measure of the efficiency of the vasomotor cells. The percentile rise obtained on stimulation of the sciatic nerve does not lessen as the initial pressure falls, but increases; and this protective action goes on until the blood pressure sinks to the level at which the bulbar and spinal cells become anemic and can no longer do their work.

Before the blood pressure has fallen so low, *i. e.*, before the bulbar cells have been made too anemic, the injection of normal saline solution is of advantage. It is true that the greater part of such an injection finds its way into the portal system and the liver, and only a small part enters the general circulation, but the heart is stimulated and oxygen-bearing corpuscles are carried to the bulb in somewhat greater numbers. When, on the other hand, vascular dilatation is excessive, vast numbers of red corpuscles are withdrawn into the veins where, so far as the bulbar cells are concerned, they are as effectually lost as if they were outside the body. The central nerve cells are very rapidly injured by the lack of oxygen, and their recovery from oxygen starvation is difficult and slow. At this stage, saline injections are of little help. Hemoglobin carriers are needed and transfusions of blood are likely to be more useful.

It has sometimes been suggested that shock is indicated by an abnormal reflex, the blood pressure falling instead of rising on stimulation of the sciatic nerve. Even a fall would indicate that the vasomotor cells were not exhausted, though it would point to a disturbance of their normal equilibrium. This reversal of the normal reflex, however, often occurs when the blood pressure is at the normal level, and when signs of shock are

absent. It can be produced by strychnine, chloral, or curare.

The experiments of the writer and his co-workers were necessarily made from the usual laboratory animals. It may be objected, by those who are not well versed in experimental physiology, that the symptoms of shock in the cat or rabbit cannot have the diagnostic value of the identical symptoms in man, because of the differences between man and these lower animals. These differences are marked indeed, but they should not be made the basis of a hasty generalization. It is conceded that skilled movements, for example, are much more highly developed in man and in the anthropoid apes than in such animals as the rabbit and the cat. But experience suggests that the maintenance of blood pressure, like the respiration, belongs to those fundamental functions that are singularly alike in all the higher animals. The fact has already been mentioned that the vasomotor reflexes are essentially identical in the cat, rabbit, rat and hen. As the difference in structure between the cat and the hen, for example, is greater than the difference between the cat and man, it would seem safe to conclude that the vasomotor reactions in man are essentially like those in other high mammals.

A clear distinction should be made between the symptoms of shock and shock itself. The symptoms of shock form a clinical entity about which there can be little dispute; shock, on the contrary, is a pathological state, the data of which are at present hypothetical.

The hypothesis which constitutes the hitherto generally accepted definition of shock declares that the vasomotor cells are depressed, exhausted or inhibited by excessive stimulation of afferent nerves. The fall in blood pressure and the accompanying symptoms are declared to be the result of this depression. The experiments cited above demonstrate that the vasomotor cells are not thus depressed or inhibited and that the excessive stimulation of afferent nerves does not materially lessen the blood pressure. The present hypothetical basis of shock is thus removed. The thoughtful reader will hardly quarrel with this conclusion; he will remember that there is as yet no proof that either the respiration or the temperature can long be altered by afferent impulses.

The literature of this important subject is marred by much loose thinking. There is no conclusive evidence that any of the cases recorded as shock are justly so classed. A symptom-complex exists beyond question, but it would be hard to deny that the changes in the heart-beat and temperature as well as the apparent alteration in the nervous system are not produced by the low blood pressure.

Let us now briefly examine certain sources of error.

Many clinicians would have us believe that every case in which the blood pressure falls far below normal is shock. But this fall can readily be brought about without any injury to or pathological change in the central nervous system. Exposure of the intestines is a frequent means of

bringing about so-called shock. Now exposure of the intestines inevitably dilates the largest vascular area in the body. The general blood pressure thereupon necessarily falls. Primarily, this is not shock at all, but simply an hydrostatic phenomenon, identical with the fall in arterial pressure produced in a rubber and glass model of the circulation by reducing the peripheral resistance. It may indeed be very dangerous,—a rabbit may be bled to death in its own portal system by dividing both splanchnic nerves,—but the cause of death is anemia of the bulbar cells; a local anemia. The removal of large portions of the skin acts also primarily in this hydrostatic way by dilatation of extensive vascular areas.

A fall in blood pressure which is really due to inhibition of the heart is often attributed to a reflex lowering of the blood pressure through the action of afferent impulses on the vasomotor centers. In the human subject it is usually impossible to determine with certainty whether the alteration in the heart-beat is primary or is secondary to abnormally low blood pressure. Contrast the two following cases, the first of which occurred in the practice of a well-known surgeon, while the second was observed in the laboratory by the writer and Mr. Richardson.

In operating on a sarcoma, a "mass of glands in the neck had been freely exposed by the high incision and was readily enucleated. Several large branches of the brachial plexus, however, were spread out over the growth, and a secondary division of this portion consequently was necessitated; when this was done, the patient's radial pulse immediately became impalpable. It continued thready and almost imperceptible during the remainder of the operation, which was rapidly completed, and for almost twenty-four hours afterward."

The second instance was as follows: A rat was etherized and the carotid pressure written with a membrane manometer. A small quantity of very dilute curare solution was injected slowly into the external jugular vein. The blood pressure was now 70 mm. The difference between diastolic and systolic pressure was about 20 mm. On stimulating the brachial nerves, the individual heart-beats almost disappeared from the curve, the blood pressure fell 20 mm., and the writing lever traced an almost unbroken line. On injecting warm saline solution, the heart improved and the difference between systolic and diastolic pressure rose to about 15 mm. An effort was now made to stimulate the central end of the already divided sciatic nerve. When the severed nerve was gently raised upon a thread, the heart again failed, and the above phenomena were repeated. Thirty-six minutes later, a saline injection was given, the heart gradually recovered, the blood pressure rose to 110 mm., and stimulation of the brachial and sciatic nerves caused a rise of about 20 mm. Hg.

The clinical picture in these two cases was the same. The graphic record showed that the symptoms in the second case were due to reflex inhibition of the heart. A like explanation probably holds good for the first case. It is at least

certain that this first case cannot be used as evidence of vasomotor inhibition.

The action of concussion of the brain upon the vasomotor cells is of interest in this connection. In experiments 3 and 21, performed by the writer and Dr. Storey,¹⁴ a heavy blow on the skull caused the blood pressure to fall 70%. In five observations, the level reached by the descending pressure averaged 33 mm. Hg. This is about the level to which the blood pressure sinks after the destruction of the spinal cord. It seems probable, therefore, that the concussion produced by the blow on the skull threw out of function, for a time, the bulbar vasomotor center, producing an effect equal in degree to the severing of the vasoconstrictor paths in the cord. The anemia of the bulb thus caused is a highly dangerous condition, the persistence of which for a very short period would greatly injure the bulbar cells. The recovery of vasomotor tone under these conditions would be very slow. Unquestionably, the loss of tone due to excessive mechanical vibration of the vasomotor cells from blows on the skull or other agitation of the liquid contents of the cranio-vertebral cavity, is often classed as shock.

These three sources of error throw doubt upon the interpretation of the clinical histories examined by the writer.

The experimental data outlined in these pages are valuable in removing misconceptions and in giving greater precision to the problem, but the material at hand does not justify any theory of the mechanism of shock.

The vasomotor nervous system seldom, if ever, dilates or constricts all the vessels at one time. The same afferent impulse will cause the vasomotor center to dilate the vessels of the face while it constricts those of the abdomen. The effect upon the general blood pressure depends upon the relative size of the dilating and constricting areas. Here the splanchnic nerves, which govern the vessels in the abdomen, have great importance. Shock must therefore be studied from a local as well as a general standpoint.

The necessity of studying the parts, as well as the whole, will be more apparent when the reader remembers that the vasomotor system is composed of three separate neurons,—one in the bulb, a second in the spinal cord, and a third outside the cerebrospinal axis. Experiments¹⁵ undertaken by the writer and Dr. Clark show that the several neurons are essentially individual in their action. Were they all of one order, they would react equally to the same stimulus. In other words, the sciatic reflex and the depressor reflex should both be increased or both be diminished by the action of the same agent. We find, however, that they are affected in different ways by the same drug. Curare, for example, affects the depressor reflex in one way and the sciatic reflex in another. The experiments seem to establish a specific difference between the bulbar and the spinal motor cells. Support is given this belief by the percentile curves published by the writer on page 404, vol. 20, of the *American Journal of Physiology*. The brachial and sciatic curves differ

from the depressor curve. This matter is of great interest because it justifies the hope that a therapy of the vasomotor cells may later be established.

The individual action of peripheral areas is being studied by the writer and Dr. F. H. Pratt.¹⁰ We have thus far busied ourselves with the effect on peripheral areas of impulses derived from the blood vessels themselves. An artificial circulation is established through the hind limb of a cat and the flow measured by a counter which records the drops flowing out of the femoral vein. All connection between the blood vessels in the limb and those in the body is shut off. If the carotid artery be now opened, the general blood pressure will fall sharply. The vessels of the isolated limb will then constrict. If the general blood pressure be sharply raised, the vessels in the isolated limb will dilate. Thus variations in the general blood pressure give rise to a protective reflex, tending to raise the blood pressure when it has fallen, and to lower it when too high.

The more the circulation is studied, the stronger is the conviction that it is not a fixed state, but a sensitive equilibrium, the result of the constantly varying action of a great number of factors. Hence the difficulty of the subject and the necessity of separating the complicated mass problems into simpler problems, capable of answer one by one. Such a separation can be accomplished only in the laboratory, and it is to experimentation upon animals that we must chiefly look for new knowledge in this field.

REFERENCES.

- ¹ The technic of these experiments is described by the writer in the *Am. Jour. Physiol.*, 1907, xx, p. 399.
- ² See the review of Quetelet's *Lettres sur la théorie des probabilités* by Sir John Herschel, *Edinburgh Review*, 1850, pp. 1-57.
- ³ W. T. Porter: *Am. Jour. Physiol.*, 1907, xx, p. 401.
- ⁴ These figures may be changed slightly by the addition of new material.
- ⁵ W. T. Porter and T. A. Storey: *Am. Jour. Physiol.*, 1907, xviii, p. 181.
- ⁶ W. T. Porter and W. C. Quinby: *Bost. Med. & Surg. Jour.*, 1903, cxix, p. 455. *The Am. Jour. Physiol.*, 1907, xx, p. 501.
- ⁷ W. T. Porter, H. K. Marks and J. B. Swift, Jr.: *The Am. Jour. Physiol.*, 1907, xx, p. 444.
- ⁸ Reported to the American Physiological Society, in January, 1908.
- ⁹ *Am. Jour. Physiol.*, 1907, xx, p. 399.
- ¹⁰ It is probable that the brachial nerve will be found to be like the sciatic nerve when the number of observations is increased.
- ¹¹ Reported to the American Physiological Society, in January, 1908.
- ¹² G. W. Crile: *The blood pressure in surgery*, 1903.
- ¹³ The initial blood pressure was mentioned in nineteen instances and the blood pressure during shock in twenty-five.
- ¹⁴ W. T. Porter and T. A. Storey: *Loc. cit.*, p. 195.
- ¹⁵ Reported to the American Physiological Society, in January, 1908.
- ¹⁶ *Ibid.*

Original Articles.

THE CLINICAL IMPORTANCE OF THE UNEVEN DISTRIBUTION OF HYDROCHLORIC ACID IN THE GASTRIC CONTENTS.

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UNTIL recently one assumption has underlain all the quantitative work done on the gastric contents. A test meal of one sort or another was given, and after a definite interval of time had elapsed, a sufficient quantity was withdrawn, and,

among other things, the total acidity and the free hydrochloric acid determined. The assumption that underlies all these methods is that the chyme so obtained offers in every respect a fair sample of the total stomach contents. Certain methods in particular depend fundamentally upon this assumption. This is the case, for instance, with the method of Matthieu and Remond¹ for determining the total quantity of the gastric contents. The contents, so far as possible, are withdrawn. Thereupon 400 cc. of distilled water are introduced into the stomach, intimately mixed with what remains and again withdrawn. A comparison of the acidity of the original chyme with that so diluted will give us, by a simple calculation, the total quantity of gastric contents, but obviously only if the portion remaining in the stomach has the same acidity as that first expressed. Sahli's² otherwise very ingenious utilization of the fat remaining in the stomach after the ingestion of a flour and butter soup, since it involves the use of Matthieu and Remond's method, is based upon the same assumption. The same is true of Strauss's specific gravity method. Practically all the textbooks are silent upon this point. Even Boas³ in the English 1907 edition of his work on "Diseases of the Stomach" fails to mention this possible source of error.

This is the less excusable since, within the last few years, some very important work has been done on the lack of homogeneity of the gastric contents. Some twenty years ago Ellenberger⁴ and his pupils showed that when horses were fed first hay and then oats, these two substances, instead of being intimately mingled in the stomach, remained separate, in distinct layers, nearly to the end of gastric digestion. Similar results were obtained with dogs and pigs and seemed definitely to disprove the existence of homogeneous stomach contents, at least in these animals. Unfortunately these observations were ignored for many years, both by physiologists and by clinicians; perhaps because they appeared chiefly in veterinary journals. They have recently been amply confirmed by Scheunert⁵ and especially by Grutzner.⁶ The latter fed various animals (frogs, rats, rabbits, dogs, etc.) with food, the successive portions of which were of different colors. At varying intervals the stomachs were tied off, removed and plunged into a salt and ice mixture. The mushy contents, frozen solid and cut into sections, showed always a definite stratification. The different portions of the food, far from being intimately mingled, could be seen in layers, separate and distinct, one above the other.

All of these experiments were done with solid food. It might be thought that a liquid meal would result in greater homogeneity of the gastric contents. Prym⁷ has investigated the behavior of Sahli's flour and butter soup in this respect. Dogs were given such soup, to which blue litmus had been added. At varying intervals the stomachs were tied off, cut out, frozen solid and cut into sections. The central portion and that near the cardia were usually found still blue in color, the rest having been turned red by the