PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

On the Changes Produced in the Circulation and Respiration by Increase of the Intra-Cranial Pressure or Tension

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IV. *On the Changes produced in the Circulation and Respiration by Increase of the Intra-cranial Pressure or Tension.**

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Contents.

Introduction.

For some time we have made intra-cranial pressure the subject of an enquiry. The present paper deals with the effect upon the circulation and respiration of an increase of such intra-cranial pressure. Our object is to indicate how the degree of the intra-cranial tension may be estimated by changes in the pulse and breathing, whether a prognosis may be formed as to the termination of the condition, and whether the effect is due to gradual loss of function of the lower part of the medulla.

Until lately, the pulse and breathing have yielded signs, the meaning of which was uncertain; thus the pulse, it is said, may be slow and of low tension, or again, in severe cases, quicker than normal and of high tension. The respiration also, is sometimes noted as being stertorous, or of the "Cheyne-Stokes" rhythm. But although death frequently comes by arrest of respiration in tumours of the brain, whilst the heart may continue to beat for five, ten, or even thirty minutes after, little has been recorded concerning the abnormal rhythm of respiration preceding its arrest; we

* The expenses of this investigation were defrayed by a part of a grant of money made by the Royal Society.

† I wish to take this opportunity of saying that the bulk of the labour of making and collating the records in this research has been performed by Mr. Spencer.—V.H.

therefore arranged our experimental method so as to investigate these phenomena in their entirety. It is impossible to give a full explanation of all the results we have obtained, because the functions of the medulla are not yet fully understood, and therefore, whatever hypotheses we have advanced on these points in this paper, have been inserted merely for the sake of clearness, and are fully open, of course, to future revision. However, the recorded tracings of all the experiments show so clearly that a diminished activity of the medulla occurs as a definite sequence of events contemporaneously with increase in the intra-cranial pressure, that we regard this fundamental fact to be established; therefore the value of the results, as regards the estimation of the effect of increased pressure, is independent of exact knowledge of the mode of their production. Further, we believe that our experiments have an important general bearing, in that they show how the three "centres" regulating the heart rate, the blood pressure, and the respiration, can be impeded or arrested, either together, or almost separately, and consequently the varying influences they have the one on the other can be estimated with an approximation to accuracy.

2. *Historical Retrospect.*

Of course an immense number of researches have been made in investigation of the general subject of intra-cranial pressure and compression of the brain, but for the present purpose, with the view of avoiding confusion, we have selected only those observations which directly bear on the object of the present communication.

Lorry, in a research,* compressed the skulls of young animals and produced unconsciousness. Also, he inserted a curved instrument through the membrana obturatoria. When he pressed the cerebellum down on the medulla the animal fell into a deep sleep, when he turned the instrument round and touched the upper end of the spinal cord, the animal awoke and became convulsed.

Astley Cooper† made a very suggestive experiment bearing on this point; he trephined a Dog and pressed with his finger upon the dura mater; the Dog became insensible, then comatose, and the pulse slow. When the pressure was relaxed the animal recovered consciousness completely.

Leyden‡ was the first to record the changes in blood pressure by a series of experiments, in which he raised the intra-cranial pressure with a piston fitting into a collar which had been screwed into the skull, the pressure on the piston being measured by a column of mercury. He noted the slowing of the pulse and, later on, its great rapidity, also the deep stertorous respiration, its final arrest, and the effects of division of the vagi on the pulse rate.

* "Sur les Mouvemens du Cerveau et de la Dure-mère; 2me Mémoire." 'Mémoires de l'Académie des Sciences.—Sav. Étrang.,' vol. 3, 1760, p. 344.

† 'Lectures on Surgery,' 1824, vol. 1, p. 300.

‡ Virchow's 'Archiv,' 1866, vol. 37.

DURET* injected wax in order to increase the intra-cranial pressure. In one experiment, when he injected a large quantity of wax into the cranial cavity of a Dog, respiration ceased, but as soon as the occipito-atlantal ligament (membrana obturatoria) was incised, the subarachnoid fluid spurted out in a stream, 50 to 60 mm. high, and the Dog began to breathe again. DURET also found that when the pressure of the injected fluid was increased from 18 to 27 mm. Hg, the pulse frequently sank from 83 to 13, and the blood pressure increased to 160–220 mm. Hg, or even higher, and further, that when the pressure of the injection was 27 to 33 mm. Hg, the pulse increased in frequency. Diminution of the intra-cranial space amounting to 5 per cent. of its content, when the injection was subdural, produced somnolence and coma, and 8 per cent. decrease of the space produced death in a few hours.

PAGENSTECHER† found that the cranial cavity could be reduced by wax measuring 2·9 per cent. of its content, or even in some cases 6·5 per cent., without any symptoms being caused.

FRANÇOIS FRANCK‡ made a series of experiments which showed that (1) a sudden increase of pressure in the intra-cranial arterioles produced slowing of the heart beats, (2) the increase of intra-cardiac pressure had the same result.

For this experiment he isolated the cerebral circulation in the Dog by ligature of the four arteries in the neck and kept up an artificial circulation of defibrinated blood through the brain. When a regular rhythm of the heart appeared he raised the pressure of the circulation through the distal end of the carotid by 4 cm. Hg. The result was an arrest of the heart with a great fall of blood pressure. The arrest of the heart lasted three seconds and then the beats regained their former frequency. He further found that, even when the cerebral circulation was not cut off, if defibrinated blood were sharply injected into the peripheral end of the carotid in a Dog an arrest of the heart could be produced, and that when the artificial circulation was in action the result of obstruction to the outflow through the jugular veins was the same as when the pressure of the inflowing fluid was raised.

He also raised the intra-cranial pressure in another way.

He screwed into a trephine hole a collar which was closed below by a membrane of caoutchouc and which was connected at the external end to a pressure bottle and manometer. He employed air as the agent of compression, the membrane preventing the air from reaching the veins, and at the same time, by distending, providing for the required diminution of the intra-cranial space. He found that gradual compression of the surface of the brain produced slowing of the heart and of the respiratory movements. These effects were produced before the height of the compression reached that of the blood pressure.

* 'Traumatismes Cérébraux,' Paris, 1878.

† 'Experimente und Studien über Gehirndruck,' Heidelberg, 1871.

‡ 'Travaux du Laboratoire MAREY.'

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

BERGMANN* injected wax and found the pulse became slower as 3 is to 1·2, or as 3 is to 1, and that the blood pressure was slightly raised above the normal as 1 is to 1·1, or as 1 to 1·2. The ascent and descent of the blood pressure with each heart beat was greater than normal, and the apex of each curve more rounded, owing to the prolongation of the systole. After division of the vagi the injection of wax produced still greater rise of the general blood pressure. BERGMANN also observed the result of compressing a sacral meningocele in a Child. The Child, at first restless, passed into a deep sleep, while with further compression the slow respiration became irregular. Finally the respiration was arrested for ten to twelve seconds, and then began as in "Cheyne-Stokes" respiration, to end in another pause. Meanwhile the pulse sank from 120 or 100 to 50 or 40.

NAUNYN and SCHREIBER.†—These authors produced general increase of subdural and subarachnoid tension by injecting fluid under known pressure as measured by a mercury column. If they applied rapidly a severe pressure the pulse rate notably slowed and the respiration gradually disappeared, the respiration usually slowing before the heart. If the pressure were slight and applied slowly the respiration became slowed but did not cease, and the blood pressure was raised. If the pressure were continued and increased the respiration gradually stopped as before, and it was occasionally necessary to employ artificial respiration to prevent a fatal termination. They noticed vasomotor curves of various kinds, the chief of which were (1) rhythmical variations in the mean pressure, and (2) curves commencing while the heart was slowed and disappearing as soon as the pressure was taken off. They never seem to have got the true acceleration of the heart after long continued and severe pressure. With the slowing of the heart they do not appear to have caused much fall of blood pressure nor arrest of the heart; apparently the rise of blood pressure generally obtained was aided by the large amount of fluid which was perfused into the animal. Thus as much as 400 c.c. passed into a Dog of $9\frac{1}{2}$ kilos in $1\frac{1}{2}$ hour.

SCHULTEN‡ found in a Rabbit that when the intra-cranial pressure was raised to 140 mm. Hg, by injection of salt solution, arrest of respiration took place. When the pressure was below that of the blood all that was obtained was a small rise of the blood pressure. When this was continued, exaggerated and slowed vagal heart beats were produced. This slowing of the heart beat was converted into acceleration when the blood pressure fell and a fatal termination appeared imminent. He ascribed this to simultaneous paralysis of the vagal and vasomotor centres.

He like PAGENSTECHER and DURET, further found that the symptoms of intra-cranial pressure were produced when the cranial content was diminished by more than six to seven per cent.

* "Kopfverletzungen," 'Deutsche Chirurgie,' Stuttgart, vol. 30, 1886.

† 'Archiv für Experimentelle Pathologie und Pharmakologie,' 1881, vol. 14, p. 1.

‡ 'Archiv für Klinische Chirurgie,' 1886, vol. 32, p. 455.

Schwartze* compressed the skull in young animals (Rabbits) and observed the heart directly through an opening in the thorax, artificial respiration being maintained. He found that increase of intra-cranial pressure produced, without damage to meninges or cerebrum, immediate and marked slowing of the heart.

3. *Anatomical and Physiological Considerations.*

Before commencing a description of the methods we employed and the results obtained, it is absolutely necessary to discuss certain considerations respecting the various anatomical alterations produced by the increase of pressure, as well as the probable manner in which such pressure acted, both directly upon the surface of the brain, and indirectly upon deeper parts at a distance, *e.g.*, the bulb, &c., reflex effects being excluded by the anæsthesia.

The skull and spinal column enclose the brain and cord in a rigid cavity perforated by numerous holes. During life blood enters by the arteries and escapes by the veins, the cerebro-spinal fluid being drained off by the numerous lymphatics (*vide* Axel-Key and Retzius†) which pass out through the foramina along with the nerves and other structures. Between the arterial circulation and that in the veins, and the lymph of the lymphatics, is placed the subarachnoid fluid.

The subarachnoid space is continuous throughout the cranium and freely communicates through the foramen magnum with the space in the spinal cord. An increase of the subarachnoid fluid pressure is well known to render its absorption more rapid, at the same time that the transudation of fluid from the capillaries is diminished. Hence, when the pressure of the subarachnoid fluid is raised there will be a tendency to return to the normal tension. If the increased pressure be due to part of the subarachnoid space being occupied by a foreign body, then the return to the normal tension will be reached as soon as an amount of subarachnoid fluid, corresponding to the volume of the subarachnoid space occupied by the foreign body, has been removed by absorption. If the subarachnoid fluid pressure be raised it may reach the height of the blood pressure in the capillaries supplying the cells of the cortex of the brain. If the pressure in the subarachnoid space pass beyond this point it will diminish the blood supply to the cortical cells, and if increased further, the capillaries will become obliterated, and so the circulation in the cortex be cut off altogether.

Here then we have at once a mode in which by general increase of the intra-cranial pressure, *i.e.*, of the cerebro-spinal fluid, failure of the function of the nerve cells in the cortex is produced. This also applies, no doubt, to the grey matter of the central ventricular axis, and we believe this to occur, the more especially since the valuable

* 'Archiv für Gynäkologie,' 1870, vol. 1, p. 36.

† 'Studien in der Anatomie des Nervensystems,' 1st part, Stockholm, 1875.

results obtained by DURET* (and from which he derived his principle of "choc céphalo-rachidien") give evidence of the communication by the cerebro-spinal fluid filling the central canal, translating the pressure applied on the outside to the centres in the grey matter lining the ventricles.

Bearing closely on this point, but also far more on the next to be discussed, are the researches made by GRASHEY† into the compressibility of the brain substance. These show at once that the effect of general increase in the intra-cranial pressure must be the speedy communication of the same to the centres in the floor of the fourth ventricle.

But it also occurred to us that another and totally different *modus operandi* of pressure, producing changes in the circulation and respiration, might be found in the direct pressure of the brain substance transmitted, like all pressure in solid bodies, in a straight line to the bulb, *i.e.*, to the nerve corpuscles constituting the vagal and other nuclei.‡

If such direct pressure be produced either by a foreign body, by depression of the skull, or by hæmorrhage, the circulation in the part of the brain compressed is impaired. If the force of compression be less than the blood pressure in the capillaries, the circulation will be only impeded; if greater than that in the capillaries, the circulation will of course be cut off.

Bearing upon this point, we may now mention that in a series of experiments not yet published, in which varying pressures were made on a circumscribed portion of the cerebral cortex by discs of glass inserted under antiseptic precautions, we observed that apparently in some instances compensation on the part of the cerebro-spinal fluid enabled the capillary circulation to be completely restored. This introduces at once a new factor for consideration under the present heading, viz., the question of the time interval required for the fulfilment of such compensation. In the researches which are the subject of the present paper, we have not regarded this important point with so much consideration as the more important one of determining what are the gravest, *i.e.*, the severest alterations in the circulation and respiration produced by rapid increase of the intra-cranial pressure.

These points being clear, there remains yet another possible way in which the blood supply to a compressed part may be provided for, besides that by compensation for the subarachnoid fluid. Thus we have reason to believe that we have seen circulatory compensation brought about by a rise in the general blood pressure, and

* *Loco citato.*

† "Ueber Hirndruck und Hirn-Compressibilität." 'Sitzungsberichte der Physico-medicinischen Gesellschaft zu Würzburg,' 1885, p. 139, and 'Allgemeine Zeitschrift für Psychiatrie.' Berlin, 1886, vol. 43, p. 276.

‡ FRANÇOIS FRANCK (*v.* "History") suggested in 1877 that the effects observed were probably due to "l'action mécanique de la compression sur les éléments nerveux et à un degré plus avancé l'anémie encéphalique unie à la première influence qui l'a déterminée et qui continue à s'exercer."

consequently a restoration of function effected in spite of the persistence of the compression.

We have alluded above to the direct communication through the brain substance in accordance with the laws of the transmission of pressure through solid bodies. It will have occurred to some who have studied this question that notice should be taken of the possibility of the cerebral hemisphere, if not the whole brain, moving *en masse* when pressure is applied in the cranial cavity at any particular point. This implies the possibility, for example, of pressure on the fore part of the brain, driving the fore part of the brain back on the occipital part, and this latter on the tentorium. This leads necessarily to the possibility of the tentorium interfering notably to the protection of the subtentorial part from pressure in the region of the cortex.

All these considerations will receive in the description of our results a detailed analysis.

4. *Modes of Investigation.*

Animals.—We have used Dogs mainly, but we have also used a few Monkeys (almost invariably *Macacus rhesus*, more rarely *Macacus sinicus*), and we hope to extend our researches on Monkeys in order to make them more closely analogous to diseased conditions in Man.

Anæsthetic.—We have employed in all cases complete anæsthesia. There is, therefore, an absence of all changes due to consciousness, reflex effects, or convulsions. Ether has been the anæsthetic used, the circulation and respiration having been steadily maintained along with complete anæsthesia. The Dog was first rendered unconscious by a mixture of equal parts of ether and chloroform. Then a tube was placed in the trachea, to which a rubber tube was attached, and at the other end of the rubber tube a funnel. An ordinary sponge-bag, half full of cotton wool, received the ether, and the funnel was inserted into the sponge-bag. By drawing the neck of the bag around the funnel to varying degrees of tightness, we found that we could regulate the proportion of air to ether. In this way the narcosis can be regularly maintained in the Dog with a moderate amount of ether. Furthermore, artificial respiration was supplied through the trachea tube when required.

Mode of Recording the Respiratory Movements.—We recorded the movements of the lower part of the thorax by means of a Paul Bert's respiratory drum and tambour. This gives, of course, correctly the expansion, &c., of the chest, but does not differentiate between the action of the diaphragm and of the other respiratory muscles. In all our tracings, the up stroke of the lever takes place in inspiration, and the down stroke in expiration.

Mode of Recording the Circulation.—A recording mercury manometer was used for this purpose, connected with a cannula in the carotid. We also, occasionally, used a Fick's spring kymograph, but since every forcible heart-beat produced a violent

excursion of the lever, an accurate tracing was scarcely possible when the blood pressure rose very high. We consequently confined ourselves to the use of the mercurial manometer. Since we found that clotting frequently took place in the femoral, especially when the venosity of the blood was increased, or when there were great changes in blood pressure, we put the cannula in the carotid on the cardiac side. The cutting-off of one carotid does not, we believe, materially diminish the circulation in the brain of the Dog. The writing point of the manometer was placed vertically above or below that of the respiratory lever when at rest.

The respiratory and manometer traces were simultaneously taken on a three-metre continuous travelling smoked surface, so that the whole course of the experiment, from the application of the compression to its removal and the recovery from its influence, could be included. The rate was about 14·5 cm. per minute, and each trace is to be read from left to right.

Method of Raising the Intra-cranial Pressure.—After various attempts, we found the following the most satisfactory :—Thin-walled, easily-distensible india-rubber bags were obtained, both pear-shaped and globular. Each bag was continuous at its neck with a stiff steel thin-metal tube, about 12 cm. long and 3 mm. diameter. The other end of the metal tube was connected with the lower end of a burette by means of very thick-walled rubber tubing, which was not distensible with the pressure we employed. The burette was filled with mercury after all air had been exhausted from the rubber bag and tubing, so that when the bag was held at the level of the surface of the mercury in the burette, or rather above the level, the vacuum in the bag made it occupy the smallest possible space. When the burette containing the mercury was raised above the level of the bag, the bag immediately became distended by the mercury; and when the mercury was lowered, the bag of course immediately collapsed. If the distension of the bag were unimpeded, only a very small column of mercury was necessary to distend it, on account of the elasticity of the rubber. Therefore, when the bag was introduced into the closed skull, the amount of force required for the mere distension was neglected, as being so extremely small. Consequently, it follows that the degree to which the mercury sank in the burette, and the height of the level of the mercury above the surface of the brain, accurately represented respectively the volume of the distended bag and the degree of pressure employed. Thus the distension of the bag diminished the cranial content, and the amount of diminution was indicated in cubic centimetres by the amount of mercury which had escaped from the burette. In this way pressure on the brain could be applied slowly or rapidly, at will, to any desired amount as measured in millimetres of mercury; and by lowering the mercury column below the level of the bag, all compression of the brain could be instantly removed, and the bag reduced to occupy an inappreciable space on account of the vacuum thus produced in it.

The collapsed bag was inserted through a centimetre trephine hole, and was fixed in position by a plate of metal, perforated in the centre for the passage of the metal

tube attached to the bag. The plate closed the trephine hole, and prevented any bulging outwards of the bag or any protrusion of the brain.

The bag was inserted at various points from the supra-orbital region in front to the cerebellar region behind, as will be described later. It was first placed between the skull and the dura mater, the latter remaining intact; later, between the dura mater and the brain; and, finally, in the substance of the brain, and where necessary in the cavity of the fourth ventricle.

In order to reclose a trephine hole, a steel plug of the same diameter as the trephine was screwed tightly into it.

Another method of raising the intra-cranial pressure was to compress the skull as a whole. This, naturally, was only possible in young animals. The intact skull in Puppies was compressed for this purpose in various directions, and the amount measured by the diminution in diameter of the skull between the points compressed. As a matter of fact the results thus obtained did not differ materially from those produced by the bag pressure, and consequently are not detailed further.

The effects of intra-cranial hæmorrhage were employed as a means of pressure when the compression by the bag had injured some vessel, which bled when the pressure was removed from the bag. Also, intra-cranial vessels were intentionally divided, and the trephine hole closed through which the division had been made.

5. Results.

a. *General Observations.*

In summarising the general results we have obtained, we may first advert to the method of experiment as we found it to work practically. In the first place, if the bag were inserted between the bone and the dura mater, it was obvious from the slow distension of the bag that the separation of the dura mater from the bone was being gradually accomplished. Moreover, of course the resistance of the uninjured dura mater is considerable, seeing that that membrane shrinks somewhat when separated from the bone, and does not hang loosely, except when extensively detached. We are thus brought to consider the results of our increase of intra-cranial pressure according to the two points of view, as to whether the pressure was effected slowly or quickly. In the following experiments it will be found that we have frequently varied the rate at which the additions to the intra-cranial pressure were made. On the whole the intra-cranial pressure was applied rapidly, a maximal amount having effect generally within five minutes, and frequently within a much shorter interval.

We have next to consider the modes by which the increase of pressure on the one hand and the removal of the pressure on the other showed themselves. Although the moments of commencing and relaxing the pressure respectively were recorded on each tracing, it was from the first evident that, whereas it was comparatively easy to detect

the effects produced by the incidence of the pressure, it was by no means so easy to determine the mode of recovery after the pressure had been completely relaxed. The reason of this last difficulty we must now discuss. To those who have made observations on compression of the brain it will be easy to understand that, if the pressure applied had been considerable, and if the blood pressure were low, the brain would not react immediately upon the withdrawal of the pressure. This non-reaction, characterised by the brain remaining excavated (through the pressure of the bag, &c.), is that which we must now analyse. From other experiments, which we shall mention directly, it is clear that such excavation of the brain substance cannot of itself afford inhibitory or excitatory impulses passing down to the respiratory and circulatory centres in the medulla. This view of the facts points to the effect being due to the mechanical principles before alluded to. (See p. 205.)

That this is true is shown also by another observation which we have made in a different manner, as follows. If pressure were applied very slowly it was easy to produce a considerable amount of such excavation as that referred to, without bringing about any effects, or only slight effects which were easily recovered from.

This introduces us to the consideration of the question of *compensation* in connexion with the origin of the effect. All the experiments show that a certain diminution in the cranial cavity has to be attained before the pressure effects begin to show themselves. This preliminary diminution, measured absolutely, has we find in most of our experiments been 5 c.c. This is the average absolute diminution of the cranial capacity which must be brought about before pressure effects appear. This interesting point has been made the subject of observations, notably by Pagenstecher and Duret. These authors approached the subject from the point of view of relative diminution of the whole cavity. The chances of error in making observations of this kind are we think considerable, and demand very special attention. Although we have carefully preserved all our material, viz., brains, skulls, &c., for this object, we have nevertheless thought it best to leave the consideration of the relative values until we can devote special attention to the point: we desire, however, to consider the matter a little further on account of the remarkable constancy of the phenomenon. With our apparatus, the value obtained, *e.g.*, 5 c.c., must obviously mean the overcoming of certain resistances. These resistances we believe to be :—

1. Resistance to the outflow of cerebro-spinal fluid from the cranial cavity.
2. The resistance (*i.e.*, of the blood pressure) to the emptying of the blood vessels of the part of the brain immediately pressed upon.
3. The natural elastic resistance of the brain substance.
4. The resistance to mass displacements.

Of the last two we unfortunately know nothing, although we have commenced a research into this little known subject. Of the remaining two the resistance more easily overcome is that of the blood pressure.

In this connexion we have performed a distinct series of experiments to contribute to our present knowledge on the subject, in the following manner. Supposing the foregoing considerations to be true, it seemed clear that we could have with ease a control experiment if we first diminished the intra-cranial space by some constant amount, and then commenced the application of pressure. As might have been expected the effect was to render the bulbar centres extremely sensitive. To such a degree did this sensitiveness go, when preliminary diminution of the intra-cranial space had been carried out, that the additional diminution of 0·5 c.c. or 1 c.c. was sufficient to cause arrest of the heart.

On the other hand it became more difficult to affect the circulation and respiration, or a higher column of mercury was required to distend the bag, if more than one trephine hole were made. And this was especially the case if the dura mater were divided in addition, for then the brain bulged into the other trephine holes. Also if part of the occipital bone was removed, so that the cerebellum might bulge, or the occipito-atlantal ligament divided, and fluid could escape whenever the cerebrum was compressed, the functions of the medulla were able to recover.

The mass displacements of the brain referred to above we may now turn to. When pressure is applied to the cerebral hemisphere, especially above and in front, we have such displacement of the encephalon that in spite of the support given by the tentorium (which it is to be remembered is bony for the most part in the Carnivora) the cerebellum is driven through the foramen magnum. Consequently, the removal of the pressure effect is readily accomplished by trephining the occipital bone, and raising the vermiform process so as to lift off the compression which it is effecting upon the medulla.

Direct Mechanical Influence upon the Medulla.

We are now brought to the final consideration of a very interesting question we raised on p. 206, viz., the possibility of the pressure effect being in part due to excitation at the point of the brain chiefly pressed upon. From the facts which we have related on p. 209, there was no reason to believe that such an excitatory effect existed. But we now wish to mention a direct experiment which we made in connexion with this subject, and that of mass displacement. The experiment consisted of division of the mesencephalon, after which it was found that pressure was just as active as before in calling forth the changes in the circulation and respiration.

The effects observed are consequently not due to any local excitation at the point chiefly compressed.

b. *Details of Observations.*

The extreme difficulty of collating such an enormous number of observations as those which we have at our disposal has led us to adopt the following method of classification and arrangement of our results.

One special feature of our experiments has been the application of pressure in different regions of the brain. This we have done for a special purpose which we do not allude to in the present paper, since we do not feel ourselves to be in possession of facts, even yet, whence to draw accurate inferences. However, by moving the point of pressure we have found that additional light has been thrown upon the subject of the present paper, for the effects obtained by the application of the pressure directly to the fourth ventricle have proved so clear, that we have separated them into a distinct class of observations, and used them to explain the results of the application applied to any part of the brain. Therefore, the first great division of our results is as follows :—

Division A.—Effects of pressure applied to any part of the cerebral and cerebellar hemispheres.

Division B.—Effects of pressure applied directly in the fourth ventricle.

It next became necessary to further subdivide these primary divisions. The way that seemed most feasible to us was to take some prominent phenomenon and hang, as it were, the observations upon it. The phenomenon in question which we selected was the classical one of slowing of the heart. In this way it was possible to subdivide Division A, as follows :—

Division A.—Pressure applied to any part of the surface of the cerebrum or cerebellum.
- (1) No marked slowing of heart. . . .
  - H. Heart.
  - V. Blood pressure.
  - R. Respiration.
- (2) Slowing, arrest, and recovery of heart
  - H. Heart.
  - V. Blood pressure.
  - R. Respiration.
- (3) After division of the vagi. . . .
  - H. Heart.
  - V. Blood pressure.
  - R. Respiration.

Division B.—Pressure applied in the fourth ventricle, with consequent differentiation of pressure effects.

The observations under each sub-division are grouped according as they relate to the heart, blood pressure, and respiration, respectively.

These we have designated by the initials H for heart, V for blood pressure, and R for respiration.

We hope, therefore, in the account of our observations which we shall give immediately, that the headings of each sub-division will be comprehensible.

Division A. *Pressure applied to any part of the brain.*

(1.) Pressure insufficient to produce marked slowing of the heart.

H. *Rate of heart.*—We have observed the following changes in the rate of the

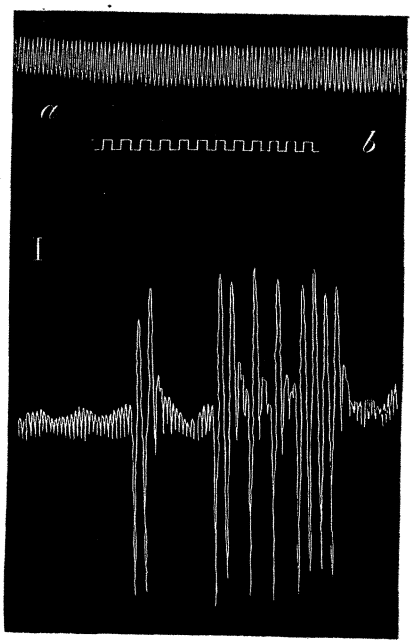
heart beat to occur under the above circumstances. A slight pressure may cause the same effect as that which results from putting the animal deeply under ether, *i.e.*, the heart rate may be diminished from 180 or 190 per minute to 130 or 120 per minute.

Less pressure is required to slow the heart when there is deep etherisation; conversely, less ether is required to arrest the respirations and slow the heart when pressure has already been applied.

Intermissions in the heart beat.—Occasionally intermissions were observed immediately on the application of the pressure, which recurred some ten times soon after the commencement. In the same experiment there were also three instances of this during the recovery from the first application of pressure.

The following experiment exhibits these phenomena (see Tracing I.) :—

Tracing I.



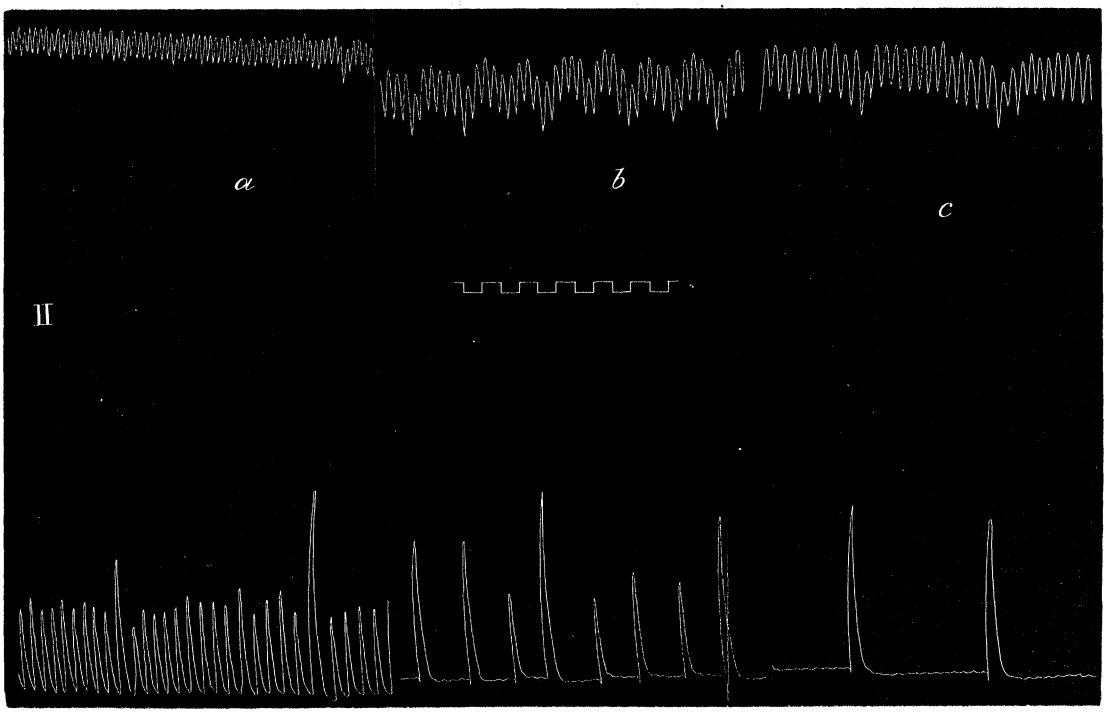
The upper line is the Respiratory tracing, the middle that of the Time, the lower that of the Blood-pressure manometer.

A. (1.) For circumstances, *vide supra.*

V. Changes in the height of the blood pressure, and the abnormal development of the respiratory variations in the blood pressure.

α. At first these variations are very slightly marked, even with the deep inspirations. As the pressure increases the variations are produced, and the curves grow longer as the respirations become slower (see Tracing II.).

Tracing II.



The upper line is the tracing of the Blood-pressure, the middle that of the Time, and the lower that of the Respiration.

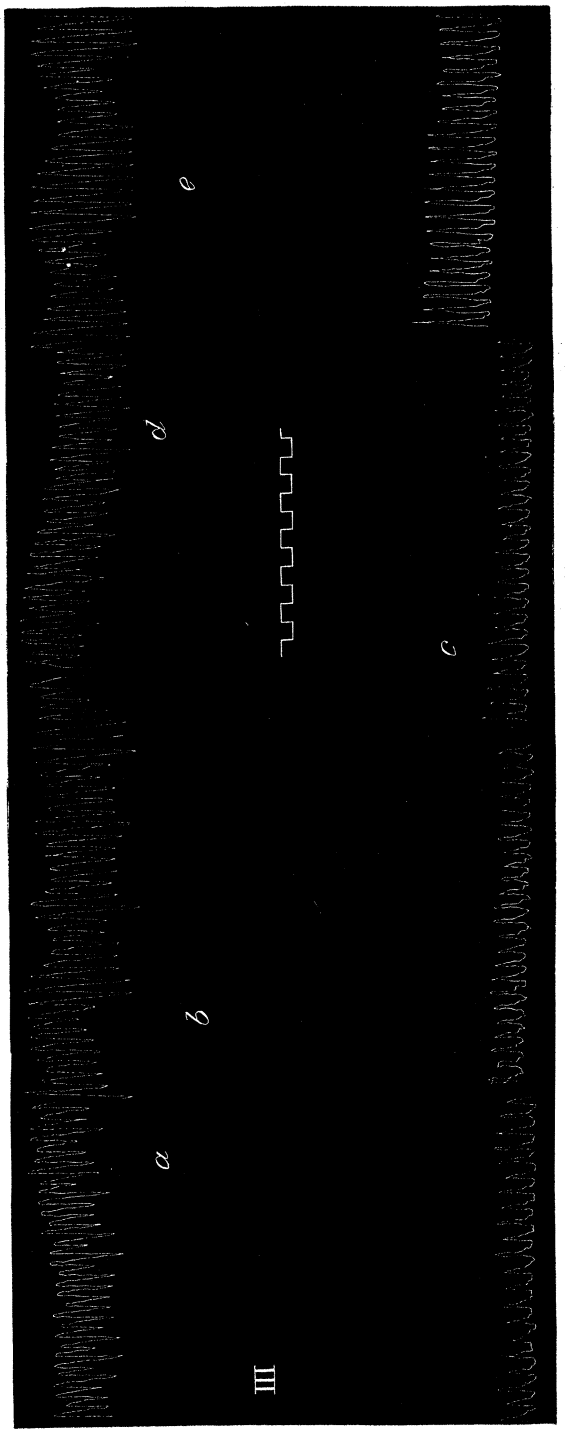
β. Vasomotor curves appearing and growing longer with the increasing pressure.

At the beginning there are none, the pressure being insufficient. But on the application of more pressure they appear, then tend to get less distinct. Additional pressure produces them again, but the curve is longer. After all pressure has been removed the curves are not seen. These phenomena are independent of the respiration and of the rate of the heart (see Tracing III.).

γ. Slight primary rise of blood pressure.

A preliminary rise of the blood pressure is never well marked in the Dog, and is only produced by putting on an adequate pressure suddenly. In the Tracing IV. this was done at the points marked 300.

In the Monkey this phenomenon of a primary rise instead of the usual fall is well marked, see Tracing V., but it would appear to be due to some pressor influence which is easily lost. Thus on repeating the application of pressure there may be no rise. In the tracing after the recovery from the first application, exactly the same pressure was again used, but here resulted the customary fall in the blood pressure instead of the rise first observed (see Tracing VI., taken from the same experiment).

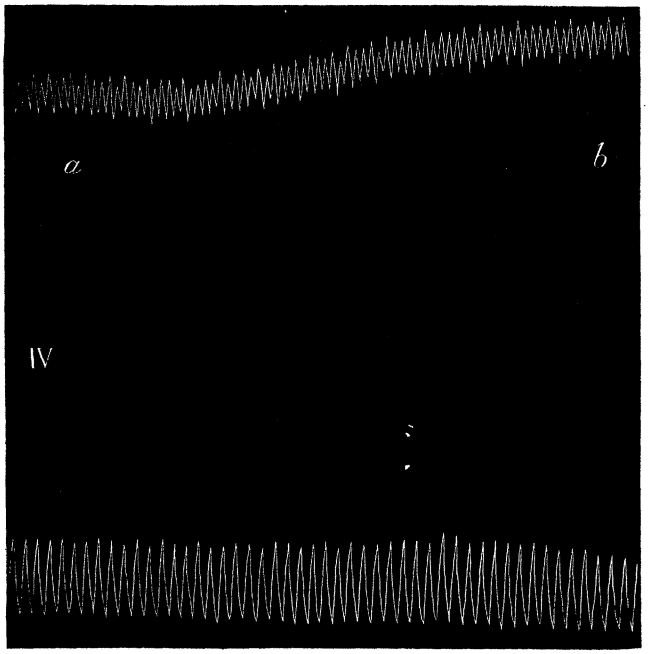


Tracing III.

The upper line is the tracing of the Blood-pressure, the middle that of the Time, and the lower that of the Respiration.

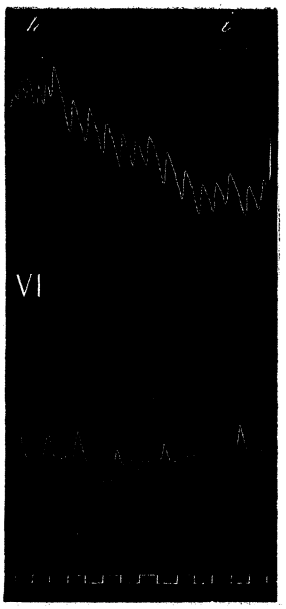
PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Tracing IV



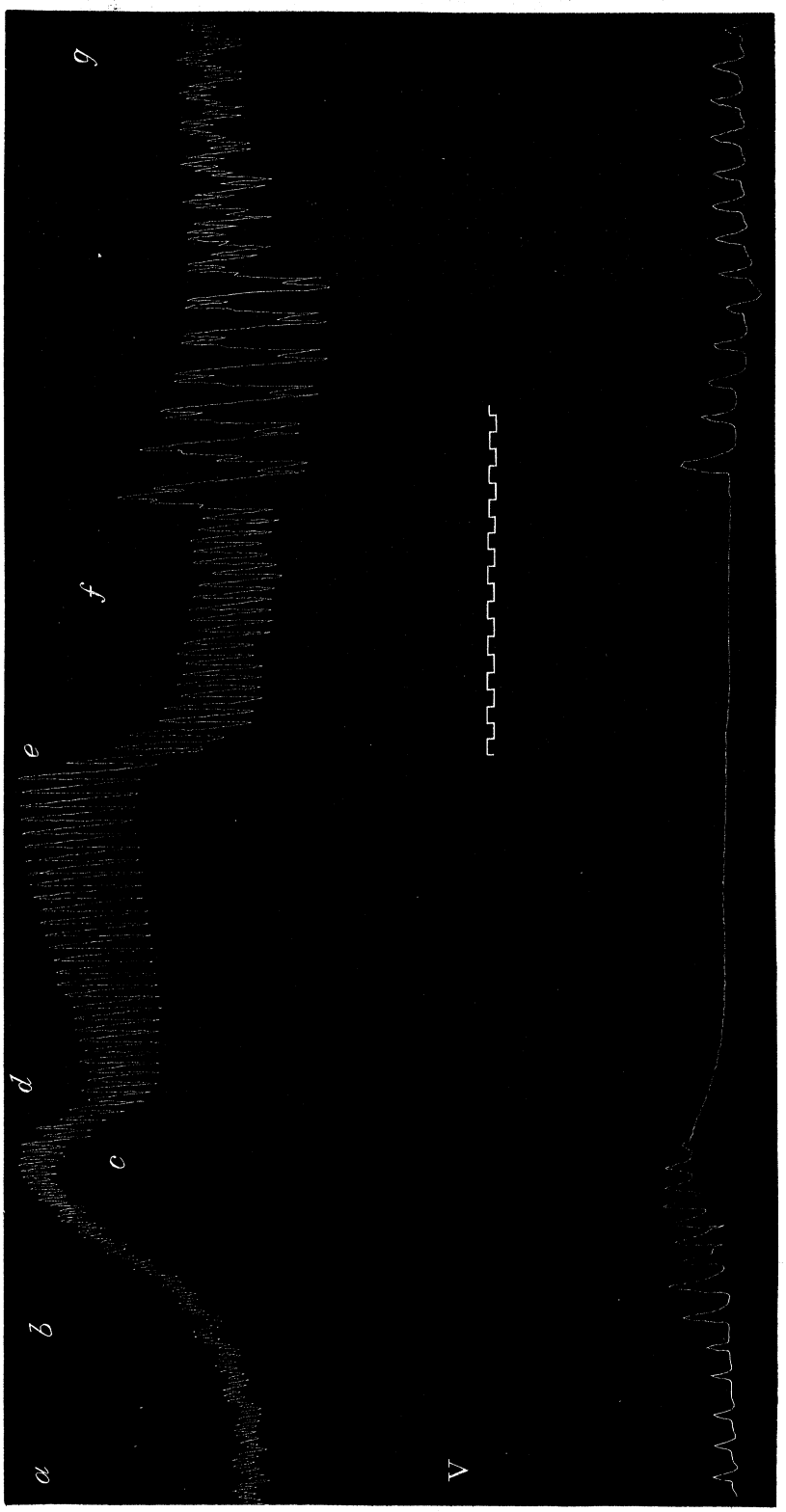
The upper line is the tracing of the Blood-pressure, the lower that of the Respiration.

Tracing VI.



The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, the lower that of the Time.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

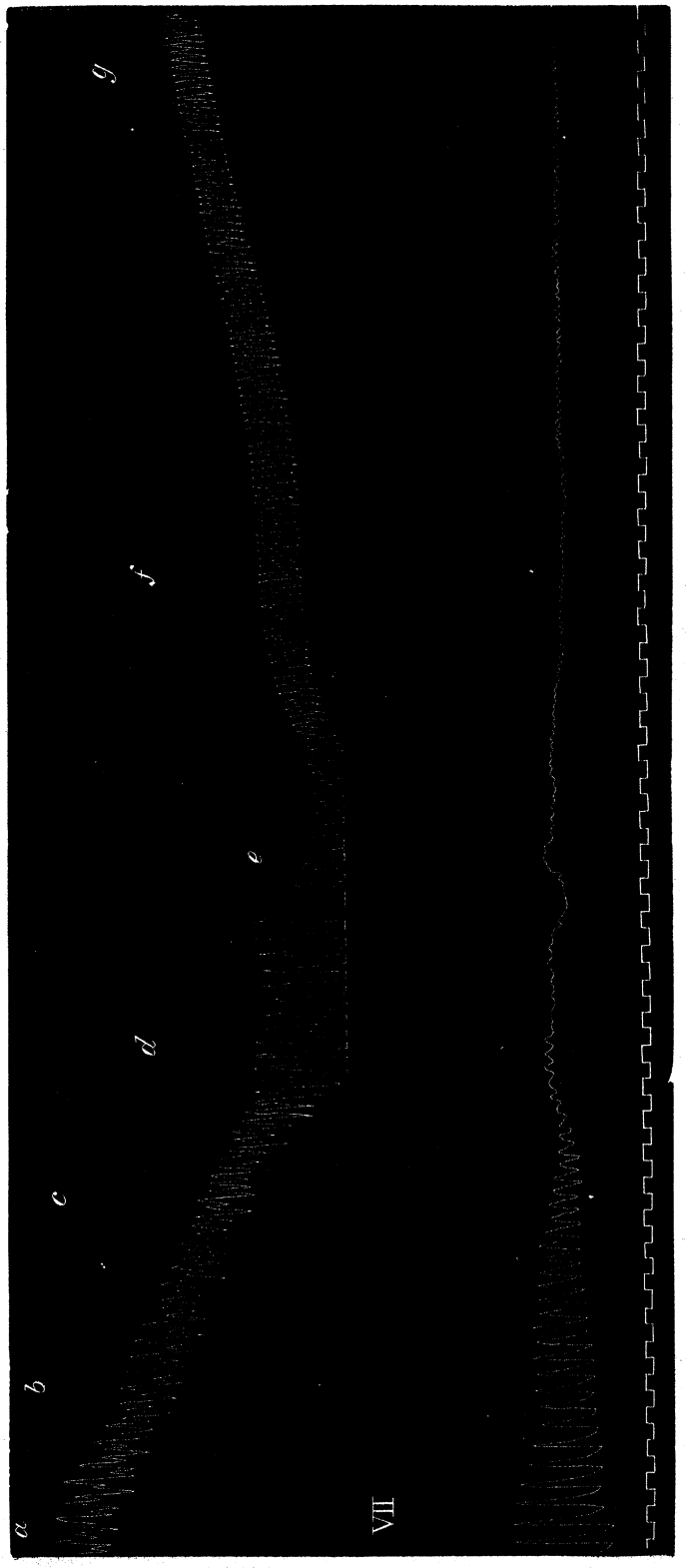


Tracing V.

The upper line is the tracing of the Blood-pressure, the middle that of the Time, the lower that of the Respiration.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Tracing VII.



The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, and the lower that of the Time.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

δ. Fall of blood pressure.

The blood pressure usually falls slightly before the heart rate is slowed. In some cases this depressor effect is very marked and apparently persists (see Tracing VII.). For, after the vagi had been divided, the rise in blood pressure was only very slow, differing much from the sudden rise which usually takes place on that operation. The phenomenon usually only occurs with the first application of the pressure, *vide infra*. This active depressor influence also occurred with an arrest of respiration, and the respiration did not begin again for some time after the pressure had been removed, and artificial respiration had been used. The connexion of these two facts will appear under B.

A. (1.) R. For the effects upon respiration see A. (2.), the effects in the present section being so slightly marked.

A. (2.) H. *Slowing, arrest, and recovery of heart.*—When pressure is applied to any part of the cerebral or cerebellar hemispheres.

α. Slowing and arrest of the heart preceded by cessation of the respiration. The respiration ceases, the heart which before was going at a normal rate is immediately slowed and is soon arrested. In such a case the effect of artificial respiration is such that the action of the heart immediately recommences, and the rhythm becomes of its former rate although the pressure is still applied, *vide β prox.*

β. Slowing increased, and arrest produced, preceded by the cessation of respiration.

In Tracing VIII. the heart on recovery is found to be still slowed.

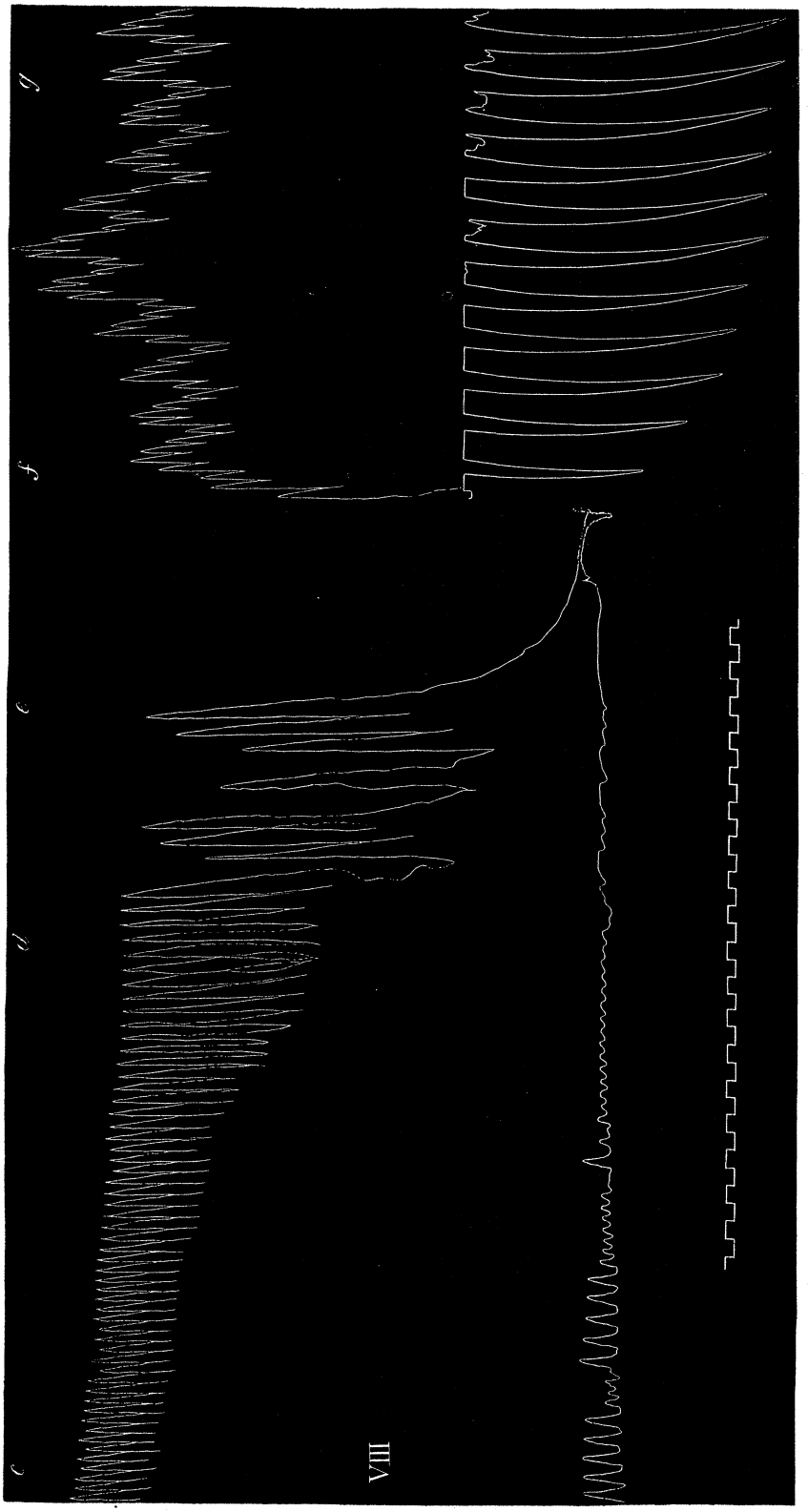
γ. Slowing of heart with arrest of the respiration; persistence of both effects after the pressure was taken off.

The heart is slowed, and the more markedly as the arrest of respiration is reached. If the pressure be removed before the slowing has led to an arrest, the heart does not immediately quicken, but remains for several beats slow. If the natural respiration then commence the heart gradually reverts to its former rate. For example see end of Tracing V.

δ. Arrest of the slowed heart occurring after the pressure has been taken off, and persisting in the presence of respiration, natural or artificial. This is shown in Tracing IX.

It will be seen that the blood pressure had shown a slight tendency to rise when the heart was arrested suddenly. The latter began again with artificial respiration.

Tracing VIII.

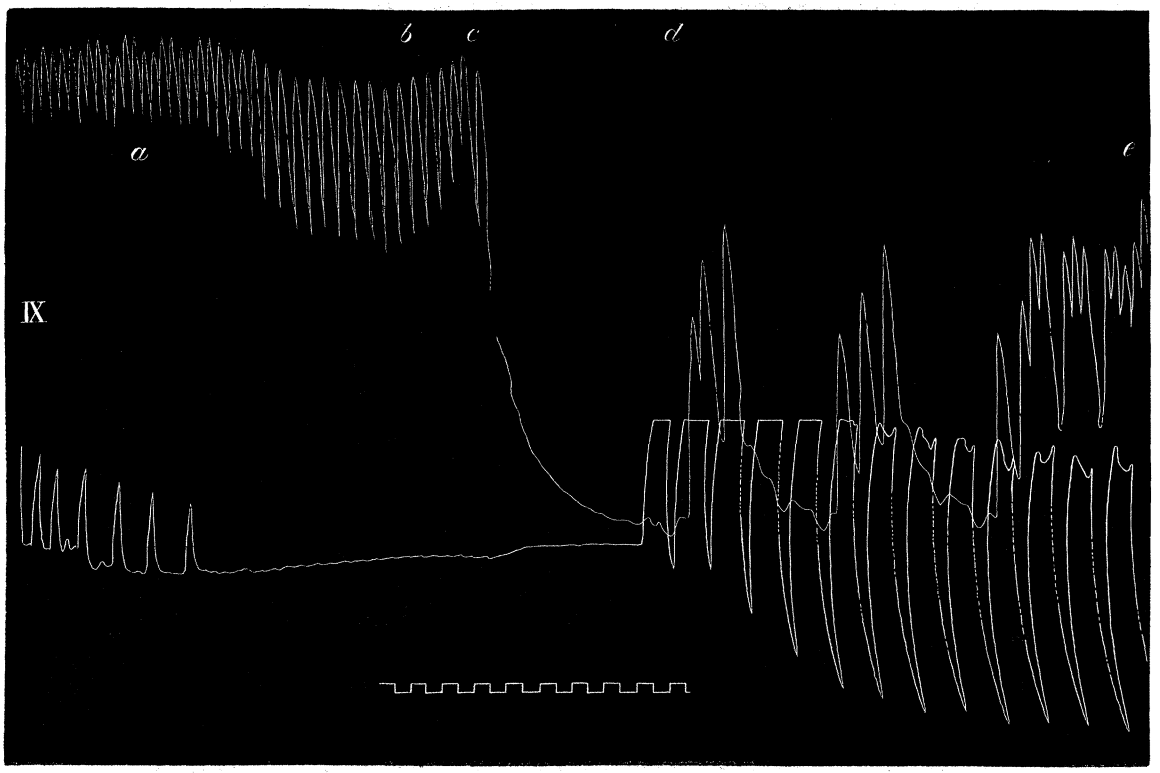


VIII

The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, and the lower that of the Time.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Tracing IX.



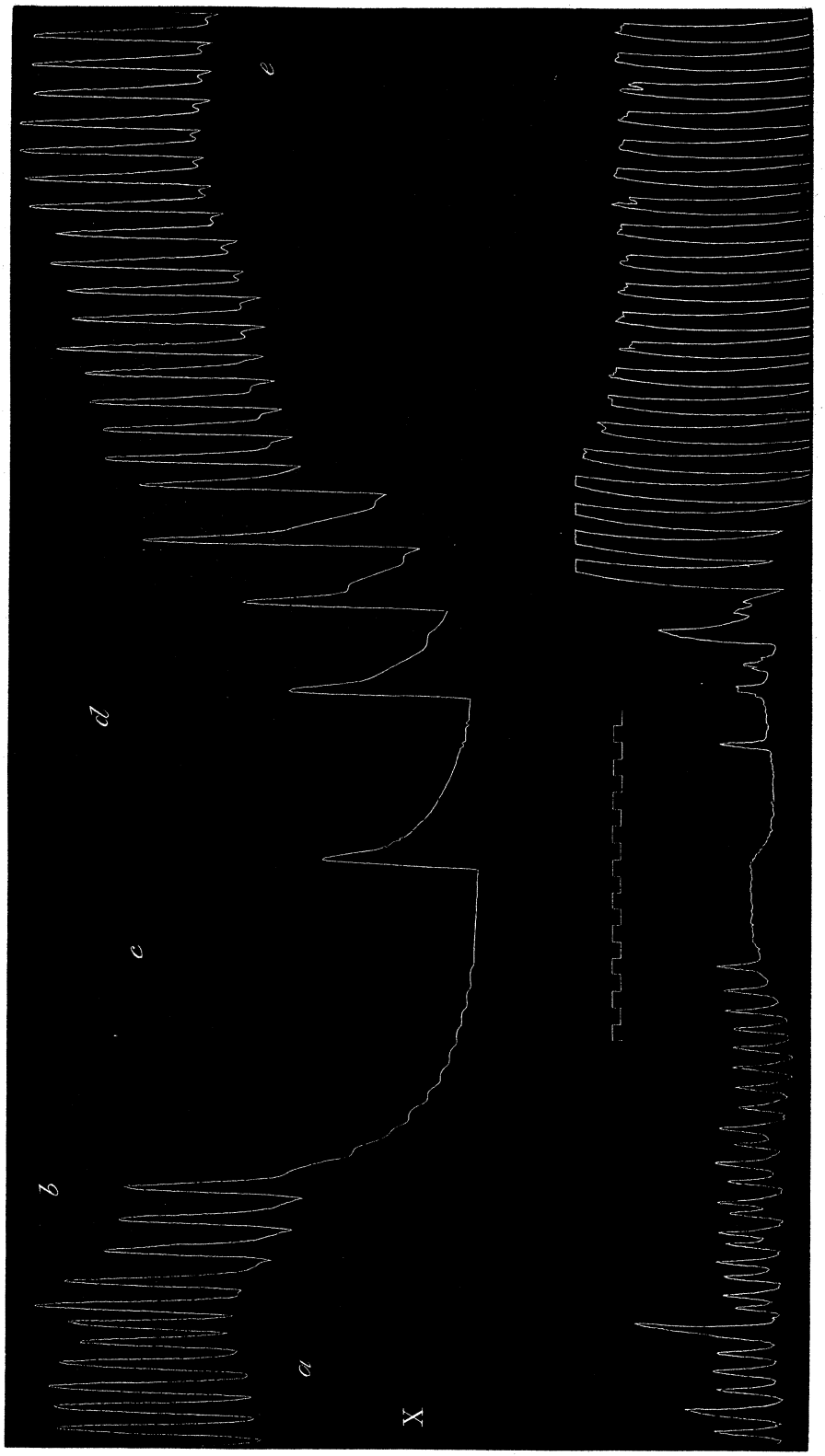
The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, and the lower that of the Time.

ϵ. Slowing and arrest of the heart; re-starting, and continuing slow.

In this case the heart was slightly, then greatly slowed, then arrested. Its arrest took place before the respiration, and continued for some time, in spite of the employment of artificial respiration. When the heart started it was at a very slow rate, and it persisted at the slow rate for a long time, during which the artificial respiration continued (see Tracing X.).

ζ. Slowing and arrest of the heart during artificial respiration; arrest continued for a long time after taking off the pressure. As seen in Tracing XI. the rate of the heart in this state became much slower, and was then suddenly arrested. It did not start again, although the pressure was taken off. Meanwhile only the weak cardiac waves excited by inflation, &c., of the thorax, caused by the artificial respiration, were to be seen in the manometer tracing (see also Tracing XII.).

After some time the heart began again, but it continued slow for a long while. Afterwards it gradually became quicker, and the artificial respirations were then



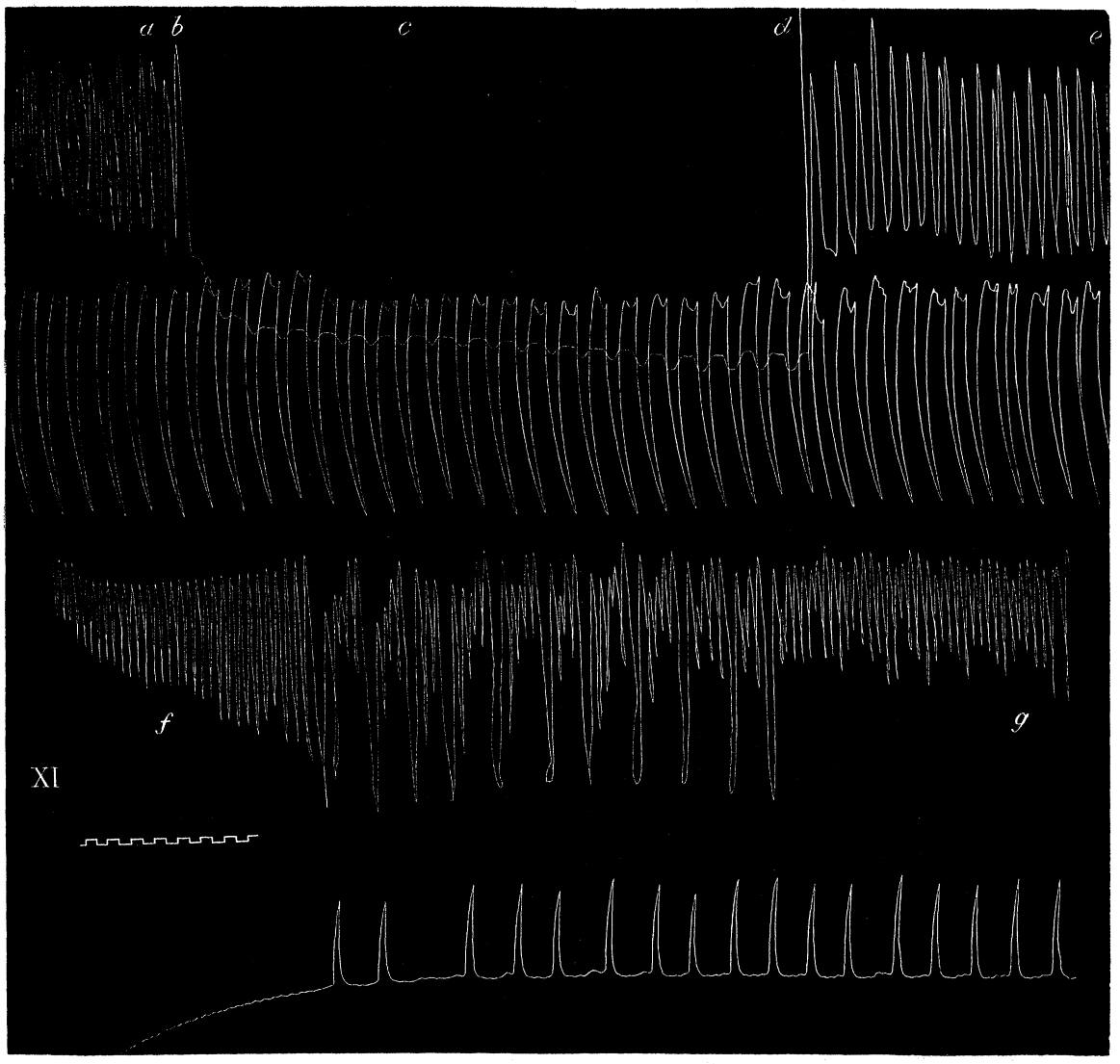
Tracing X.

The upper line is the tracing of the Blood-pressure, the middle that of the Time, the lower that of the Respiration.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

stopped. The rate again became slow, but when natural respiration began the heart rate continued to increase.

Tracing XI.



The upper line is the tracing of the Blood-pressure which is continued in the third line, the second line is that of the Respiration which is continued in the fifth line, the fourth line is the tracing of the Time.

η. Arrest of heart immediately on application of pressure, and without previous slowing.

This was only obtained purely when the bag was put into the fourth ventricle, *vide* p. 239, since with pressure applied in other places more or less slowing took place first (see Tracing XXIII.).

θ. Arrest of heart, with or without previous slowing, not starting again.

This is likely to take place when pressure is applied in the fourth ventricle, and it may happen from sudden severe pressure in other parts of the brain. Generally, however, recovery is brought about by resorting to artificial respiration.

ι. Arrest of the heart, starting again by forcible beats, separated by long intervals.

This condition of the heart's action is sometimes remarkably pronounced, as is seen in Tracing XII. After the arrest artificial respiration called forth only one beat. Next three were produced by perfusing fluid through the cannula. The heart began with large beats, separated by wide intervals. As a mode of recovery this is interesting.

κ. Increased rapidity of the heart after being slowed, the rapidity being as great as after division of the vagi, and probably due to failure of the vagal centre (see Tracing XIII.). At the left-hand side is seen the slow cardiac rate due to the pressure ; the rhythm is then seen gradually increasing in rate, until it becomes fully three times as fast, the pressure being maintained all the time. Concomitantly with the increase in rate is a rise in the blood pressure.

This condition of the vagal apparatus may (as seen in the tracing) be recovered from.

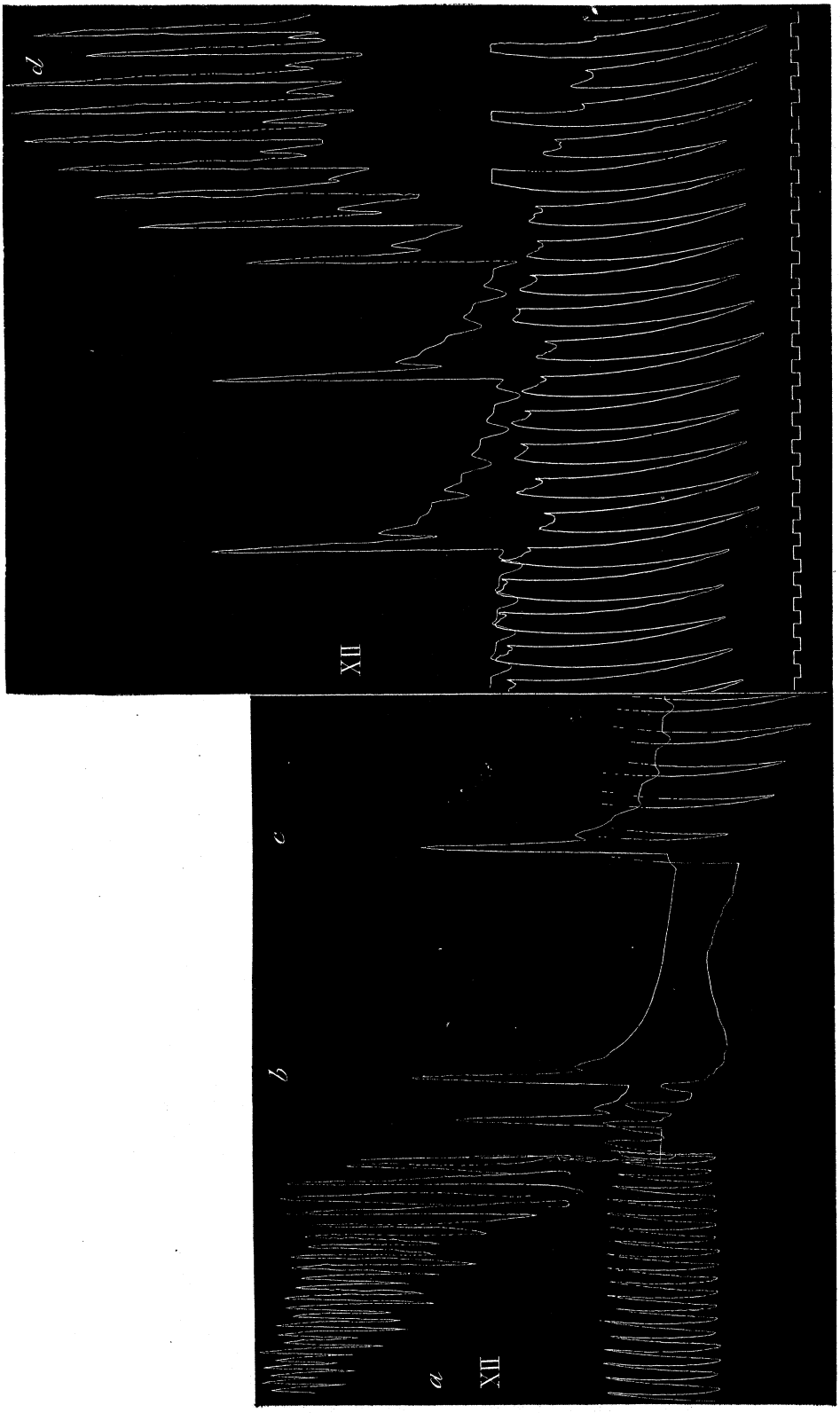
A further proof is shown in Tracing XIV., where we found that when this dissolution of the vagal centre was thus effected, subsequent division of the vagi, as might be expected, produced no change in the condition.

λ. Intermission in extent of heart beat.

This usually occurred when arrest was impending during maintenance of the pressure, but often persisted after the pressure had been removed, sometimes appeared temporarily during recovery from the effects of the pressure, or continued after the respiratory rhythm was perfectly re-established.

The rate of intermission varied from the second to the sixth beat in different cases, and had a notable tendency to fall into time with the respiratory rhythm.

We now proceed to discuss the vasomotor phenomena (V.) observed under these conditions.

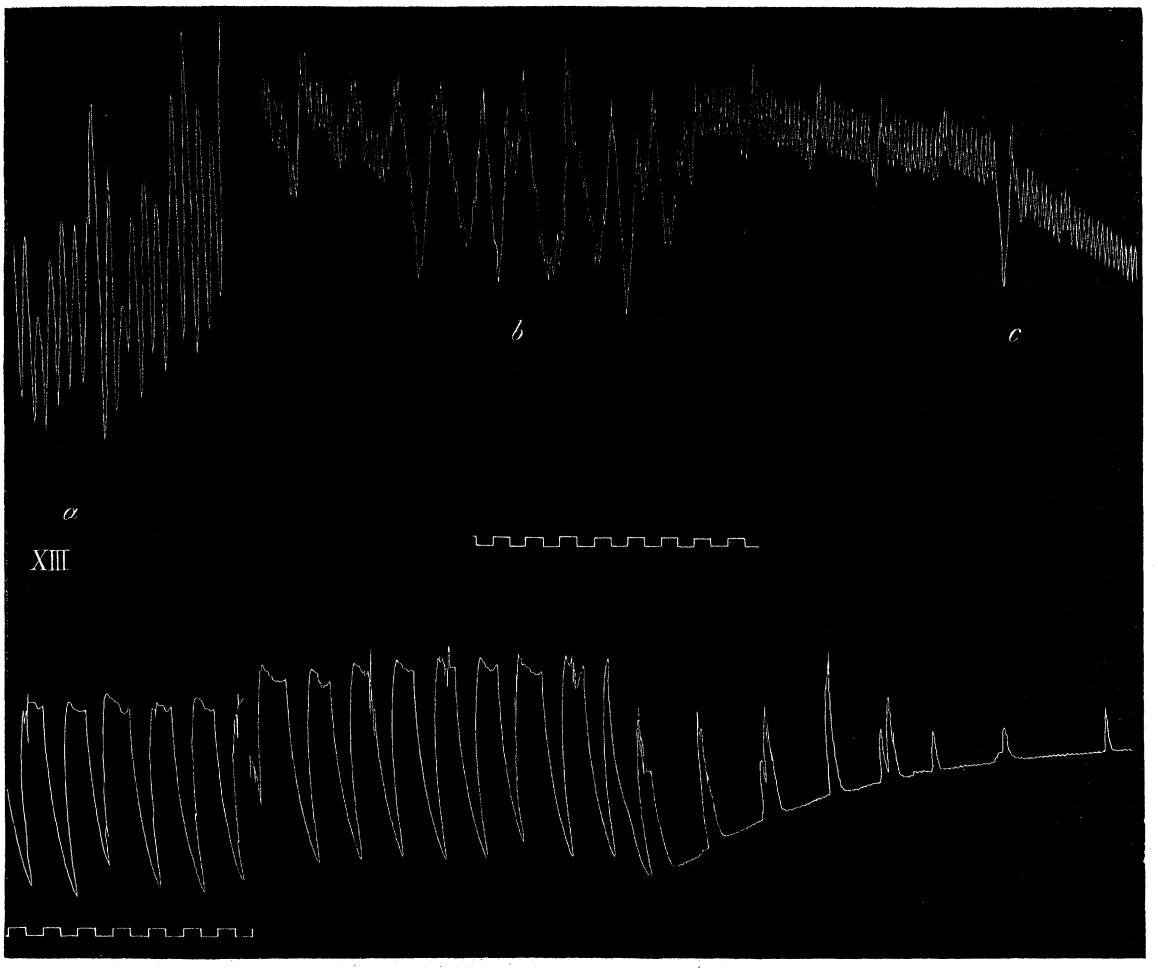


Tracing XII.

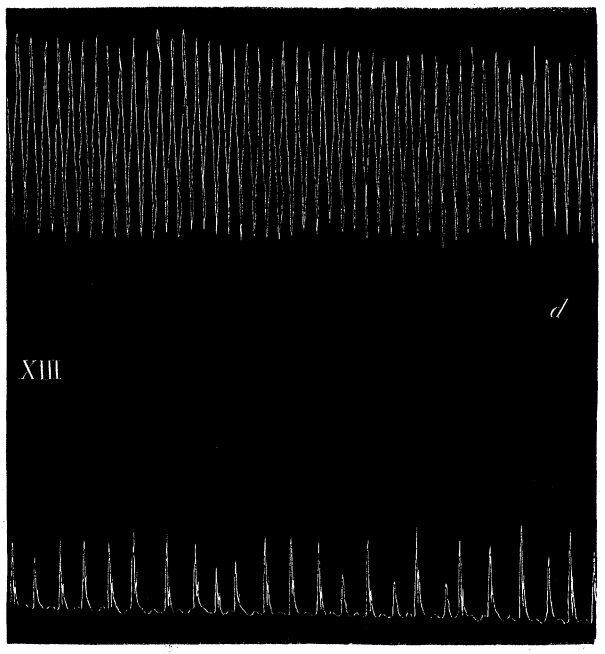
The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, and the lower that of the Time.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Tracing XIII.



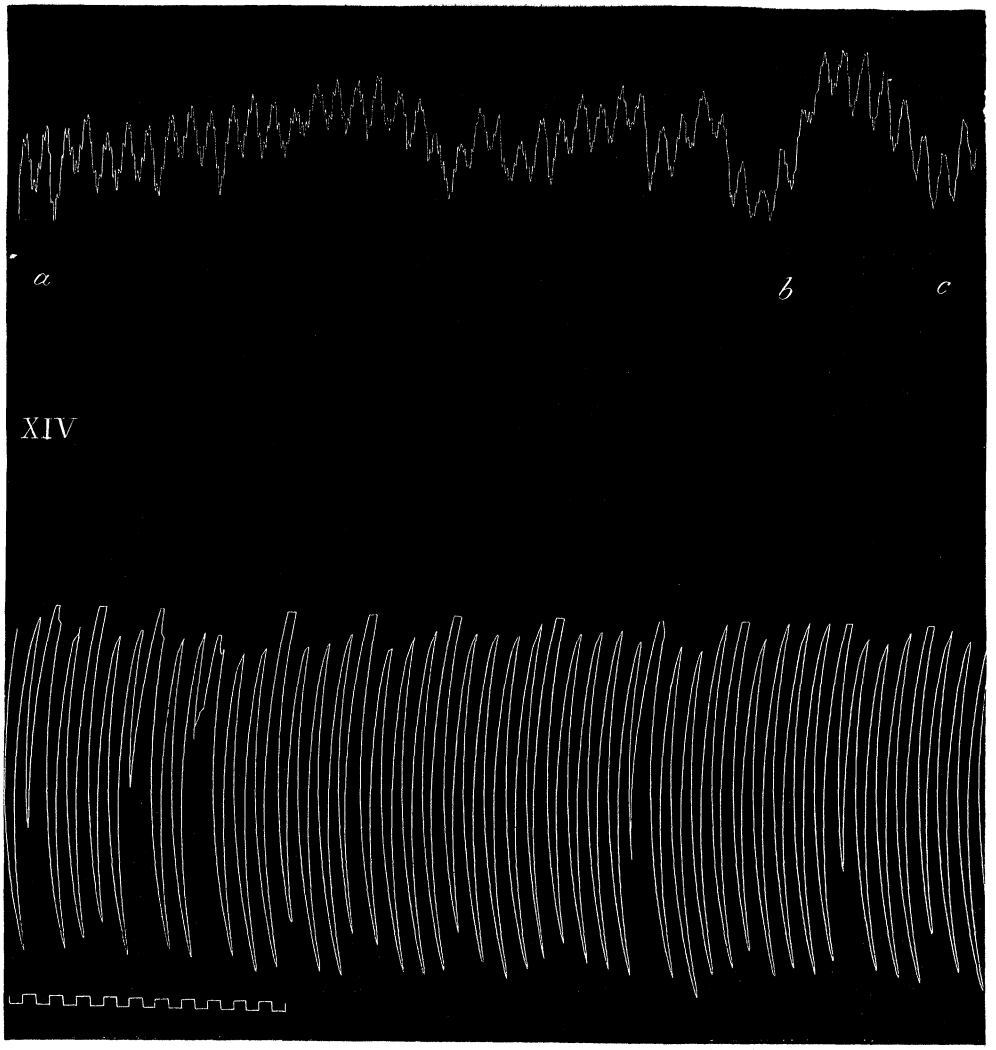
The upper line is the tracing of the Blood-pressure, the second and fourth that of the Time, the third that of the Respiration.



The upper line is the tracing of the Blood-pressure, the lower that of the Respiration.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Tracing XIV.



The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, the lower that of the Time.

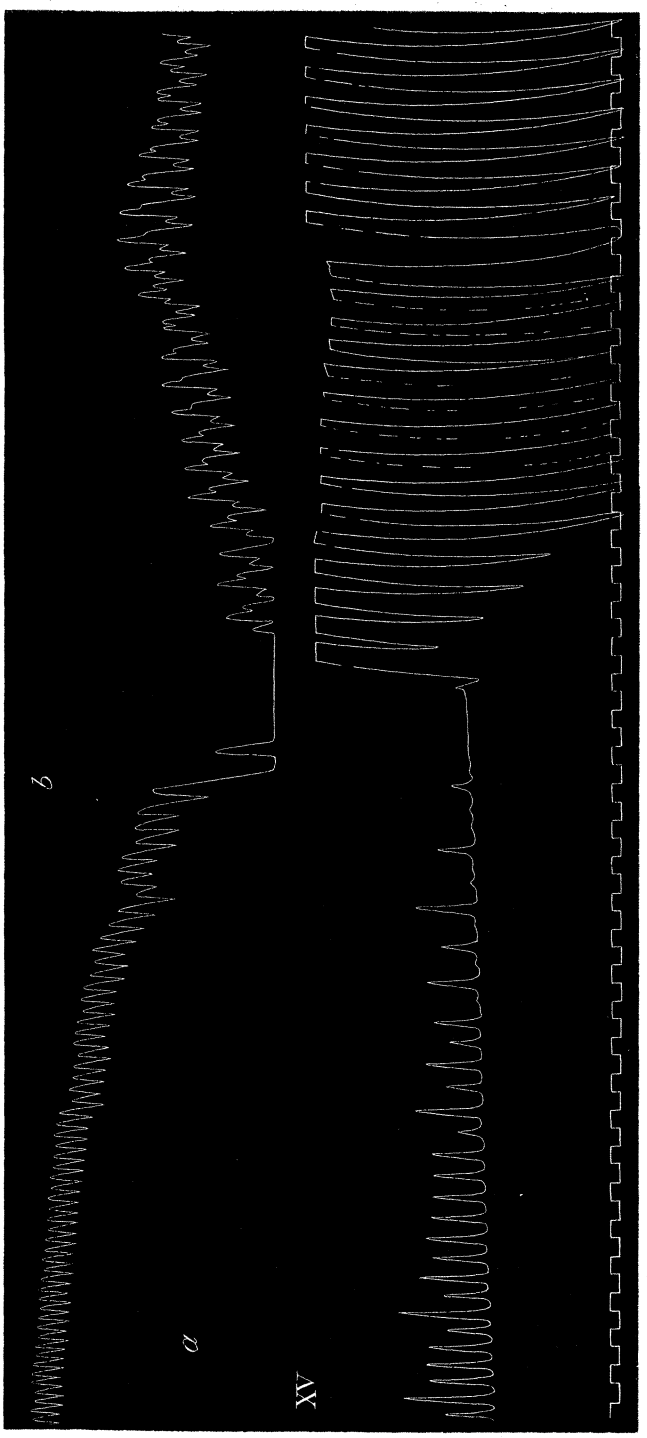
A. *Pressure applied to any part of the brain.*

(2) Slowing and arrest of heart.

V.*a*. Fall of blood pressure preceding the slowing of the heart, and continuing after recovery of the rhythmic heart rate.

In the instance shown in Tracing XV. active depressor influences caused a fall of the blood pressure before the arrest of the heart. After the return from zero the blood pressure continued low.

The same phenomenon could also be observed to continue even after section of the vagi (see Tracing VII.).

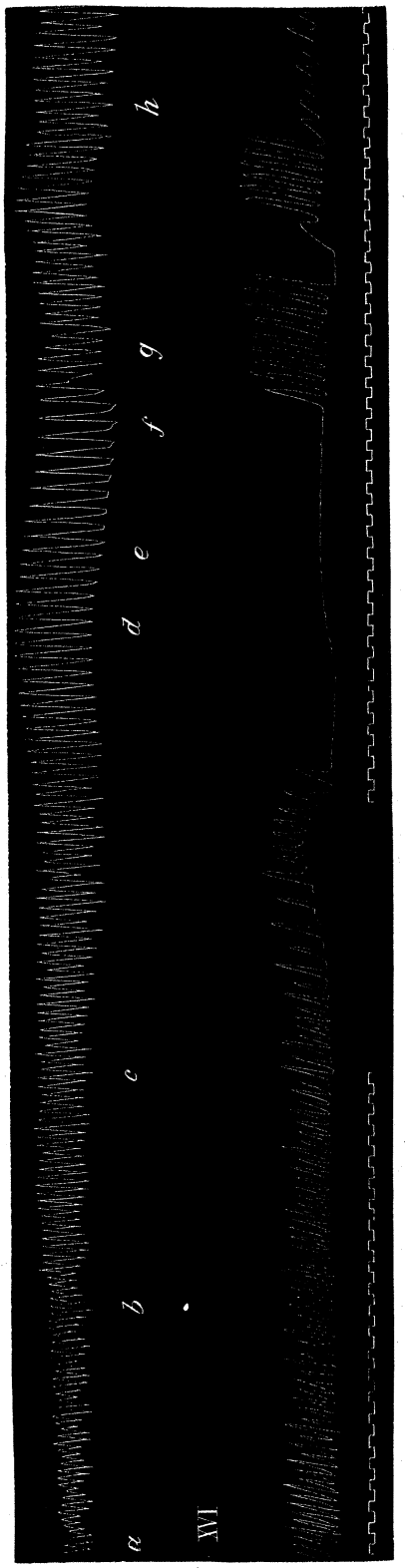


Tracing XV.

The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, and the lower that of the Time.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Tracing XVI.



The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, the lower that of the Time.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

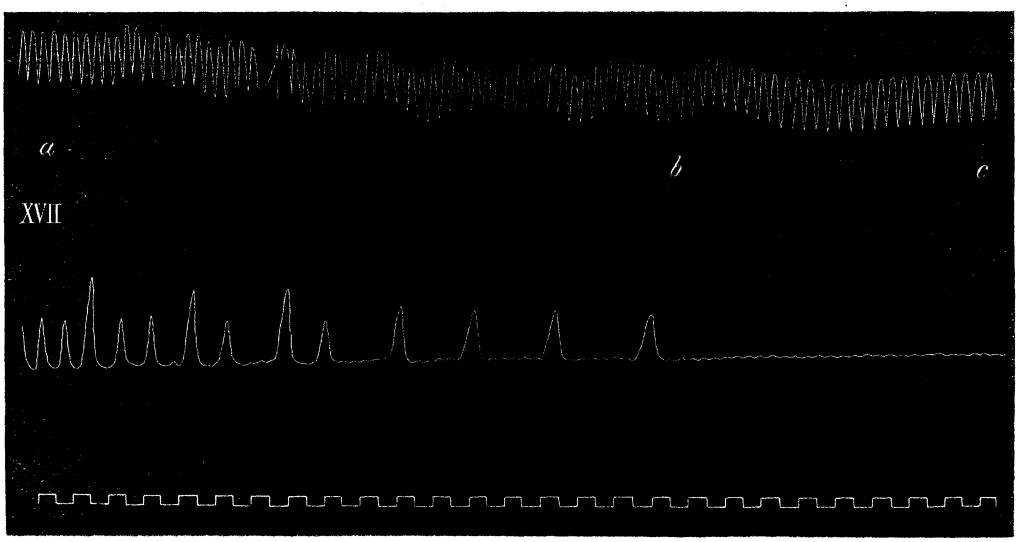
β. Depressor influences absent, although the pressure was applied for the first time, and also absent after the arrest of respiration.

This almost inexplicable fact was observed once, as seen in Tracing XVI. It is seen that, although the heart became gradually slowed down to 35 per minute, there was no fall of blood pressure. This absence of depressor influence may have been connected with the low blood pressure. That vasomotor phenomena, *e.g.*, curves, could yet be produced is seen in the tracing at *a*, where it is shown that the pressure developed vasomotor curves which continued for some time and then disappeared when the heart was slowed.

γ. Depressor influences absent when pressure was applied for the second time, after having been present on the first application.

In harmony with the foregoing this depressor influence we found to be easily destroyed in the course of an experiment, since it usually disappeared after the brain had been once compressed (see Tracing XVII.).

Tracing XVII.



The upper line is the Tracing of the Blood-pressure, the middle that of the Respiration, the lower that of the Time.

In a well-marked case the heart was only slightly slowed even after the arrest of respiration, and there was no fall of the blood pressure. This loss of depressor influence is further indicated by the blood pressure being actually above that existing before the beginning of the experiment.

In other cases the heart could be and was greatly slowed without any fall of blood

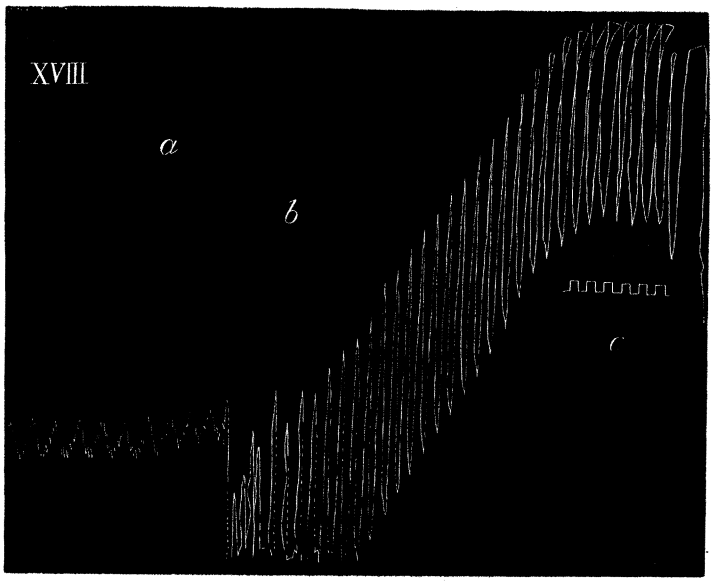
pressure, if the depressor influence had been lost during the previous application of pressure.

δ. Pressor influences causing a rise to the level attained before the application of pressure, or even somewhat higher, the heart remaining slower than usual or returning to its normal rate.

For the development of this effect (see Tracings VIII., X.) it was usually necessary to employ artificial respiration to recover the action of the heart. That it is a true vasal effect is well seen at the end of Tracing X., where the rise of pressure is obtained and maintained, although the extent of each heart beat is no greater than before.

ε. Pressor influences causing a rise considerably above the normal level, attended by either a quickening of the previously slow heart beat or by maintenance of the same slow rhythm. This is seen in Tracings XVIII., XII., XIII.

Tracing XVIII.



One line is the Tracing of the Blood-pressure, the other of the Time.

ζ. Pressor effect equal to that appearing after division of the vagi and attended by a heart rate of a similar character.

We have already shown that the heart rate under certain circumstances of intra-cranial pressure gives evidence of the failure of the bulbar vagus centre. As is shown in Tracings XIII., XIV., this is also true of the vasomotor condition which is customarily produced by section of the vagi, plus an increase of the intra-cranial tension.

η. Vasomotor curves appearing after the application of pressure.

Whereas prolonged or severe pressure abolished both respiratory and vasomotor curves, normally superadded on the manometric tracing, slight pressure occasionally *developed* vasomotor curves as is seen in Tracing XVI.

As the heart rate quickens after the temporary slowing, respiratory curves appear on the tracing, usually exaggerated at first and subsequently becoming of normal extent. (See Tracing V.)

A. (2.) R. Changes in respiration when the intra-cranial pressure is applied to any part of the encephalon, and when such pressure produces slowing and arrest of the heart's rhythm.

It will be remembered that on p. 219 we stated that the changes in respiration which accompanied only slight alteration (slowing) of the heart rate were so precisely similar to those which preceded complete arrest of the heart that we would consider them *en bloc*.

We must here allude to certain side issues connected with our method before entering upon the task of classifying and collating the results obtained.

The recording apparatus, as before stated, gave us the movements of the thoracic walls only, the ascent of the curve marking a natural inspiration or an artificial inflation of the chest. Our tracings consequently give variations in the depth of the movements of inspiration and expiration, as well as changes in the rhythm. We, however, also employed on many occasions artificial respiration; this, especially after the observations of HERING and BREUER,* is well known to notably affect the respiratory centre in the medulla oblongata. We would propose, therefore, in view of these facts, to arrange the results as follows:—

- Class I. Changes in respiration uncomplicated by artificial respiration
  - (*a*.) Changes in rhythm . . . : Inspiration; Expiration; Pause
  - (*b*.) Concomitant changes in rhythm and extent: Inspiration; Expiration; Pause
  - (*c*.) Changes in extent . . . . : Inspiration; Expiration; Both

Class II. Mode of natural recovery of changes in respiration.

Class III. Changes in respiration. Recovery as observed after the employment of artificial respiration.

* See p. 234.

Class I. Changes in respiration uncomplicated by artificial respiration.

(*a.*) *Changes in Rhythm.*—The change in rhythm is gradual, slowing as the effect of the pressure becomes more marked. The pauses become lengthened, and, as will be seen in Tracings II., XV., XVII., inspiration is deepened. If the degree of anæsthesia were light there were:—

(*b.*) *Concomitant Changes in Rhythm and Extent.*—When the rhythm is slowed as a rule the extent of the respiratory movements becomes for the time increased, but just before arrest they become shallow. (*Vide infra.*)

(*c.*) *Changes in Extent.*—The condition just alluded to is really so dependent upon the development of inspiration that it is best further considered under the head of change in extent.

On the whole the usual early effect is as a rule increase of inspiration. This inspiratory increase generally shows itself in one of two ways. Either—

(1.) By deep single inspirations occurring at fairly regular intervals. (See Tracing II.)

(2.) By an inspiratory spasm, in which it is usually seen that both expiratory and inspiratory movements have for some time been diminishing, but that just before the final arrest, expiration seems to fail, and so an inspiratory spasm is produced. (See Tracing XVI.) This spasm only lasts three or four respiratory intervals, and is followed usually by a few small double respiratory movements and then complete arrest occurs.

We can look upon this phenomenon in another way, viz., that the dissolution of the respiratory centre is signalised by failure of expiration, and so has brought about undue predominence of inspiration. In this way the influence of the pressure would not necessarily mean exaggeration of inspiration, but merely over-action in consequence of the disappearance of the antagonistic expiration. This view is suggested to us by the investigation of Richet* upon the dissolution of respiration effected by anæsthetics, he having shown that active expiration disappeared long before inspiration.

Class II. Mode of natural recovery of respiration.

The effect of the increase of pressure has been just described, it now remains to discuss the manner in which the respiratory centre begins to recover its function unaided by artificial respiration.

Rarely the respiratory movements have continued although extremely reduced in extent.

After the more usual complete arrest respiration very frequently recommences by an initial deep inspiration, and this is followed by another (gasps in fact), then successive respirations follow in increasing order of depth. (See Tracing I.)

* 'Mémoires de la Société de Biologie,' 1887, p. 25.

In fewer instances the respirations recommence not as gasps, but simply as shallow movements increasing in extent.

Class III. Changes in respiration observed after the employment of artificial respiration.

The effect of artificial respiration has usually been observed when the latter has been employed to obviate fatal results of severe pressure, consequently in every case the respiratory centre is being, or has been inhibited by pressure.

Two points call for consideration at this juncture, firstly the general improvement in the activity of the centre produced by the increased oxygenation of the blood, and, secondly, the direct inspiratory and expiratory stimuli evoked by the suction and distension respectively of the lung.*

The effects observed have been roughly divided into two categories, one in which apnœa occurred and another in which it was absent.

When apnœa followed, the respiratory movements usually commenced again, having a good depth; but when no apnœa was produced, *i.e.*, when the respirations almost immediately recommenced, the movements were shallow. This difference, however, is not to be regarded as in any way absolute.

Before passing on to the next chapter, viz., the variation in the foregoing results produced by section of the vagi, we must offer a few further remarks on the abolition of the respiratory function, especially as regards its parallelism with the arrest of the heart.

Of the two, respiration is almost invariably affected first, *i.e.*, in rhythm and extent. The arrest of respiration, however, ought not to be regarded as strictly comparable to the condition of arrest of the heart, since the latter implies excitation of a bulbar centre, whereas arrest of respiration means paralysis, *i.e.*, an effect of much greater importance.

Hence the fact that the two are arrested simultaneously (see Tracing XXIII.), or even the respiration a little after the heart (see Tracing X.), only goes to show that the respiratory centre is by far the more sensitive, and consequently, as an index of pressure, more delicate than the heart's action.

A. (3.) The variation in the effects observed to be produced by section of the vagi.

We have made a large number of observations after preliminary section of the vagi. The effect of division of one vagus was practically nil.† When it was pulled on

* Hering and Breuer "Die Selbststeuerung der Athmung durch den Nervus Vagus." 'Sitzber. d. K. Akad. d. Wissenschaft'; Wien, 1868, April, November (vol. 57, *Abth.* 2, p. 672; vol. 58, *Abth.* 2, p. 909). See also Head, 'Journ. of Physiology,' 1889, and other authors.

† We did not make special observations on this point, except to satisfy ourselves that the heart could he slowed through one vagus nerve by increased intra-cranial pressure.

slightly for the purpose of division the tension produced a temporary slowing of the heart.

Division of both vagi invariably produced the classical phenomena of—

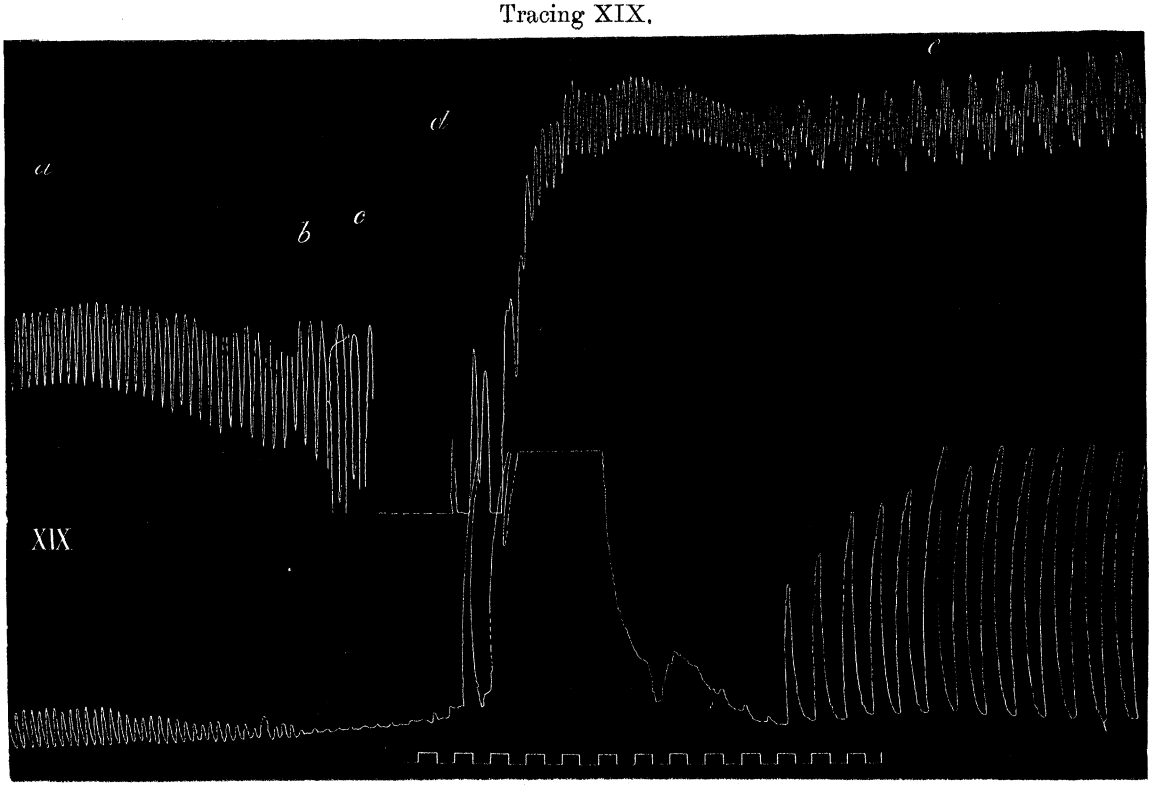
(1.) Rapid heart action.
(2.) Rise of blood pressure.
(3.) Alteration of respiration.

Following Leyden* it was obviously of extreme importance that these variations should be studied under the condition of increased intra-cranial pressure.

We therefore prepared the vagi in the usual way and divided the nerves, sometimes before pressure was applied, sometimes while it was acting.

The general results remained the same.

Tracing XIX.



The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, the lower that of the Time.

A. (3.) H. After division of the vagi the heart rate immediately became rapid and was unaltered by increase of the intra-cranial pressure, but when the latter caused a rise of blood pressure the rate was notably quickened, slowing again as the blood pressure fell.

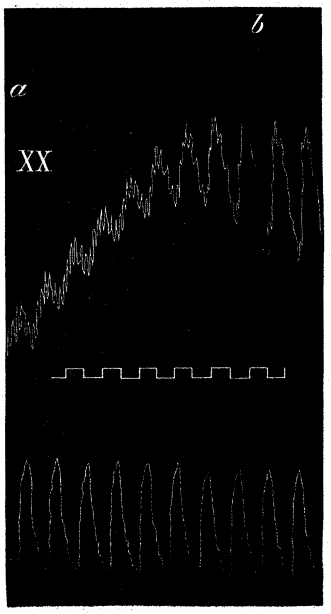
* *Loc. cit.*

The effect on the heart is thus of minor importance, but as will be now seen, the change in the blood pressure evoked by rise of the intra-cranial pressure after division of the vagi is most remarkable. (*Vide* also Historical Introduction; BERGMANN.)

A. (3.) V. Firstly it is to be noted that, after a depressor influence has been occasioned by raising the intra-cranial pressure, the effect of dividing the vagi is only to slowly develop the remarkable additional rise in the blood pressure. (*Vide* Tracing VII.)

With this preliminary notice of possible depressor effect we must proceed to describe the pressor influence, which is so eminently characteristic when the intra-cranial pressure is raised. It is sufficient perhaps to state that after division of the vagi the effect of putting on pressure is to immediately cause a rapid rise in the blood pressure. So long as the vasomotor central apparatus is intact and in functional activity, this rise continues to advance with additional increase of pressure until the extreme point now to be mentioned is reached.

Tracing XX.



The upper line is the tracing of the Blood-pressure, the middle that of the Time, and the lower that of the Respiration.

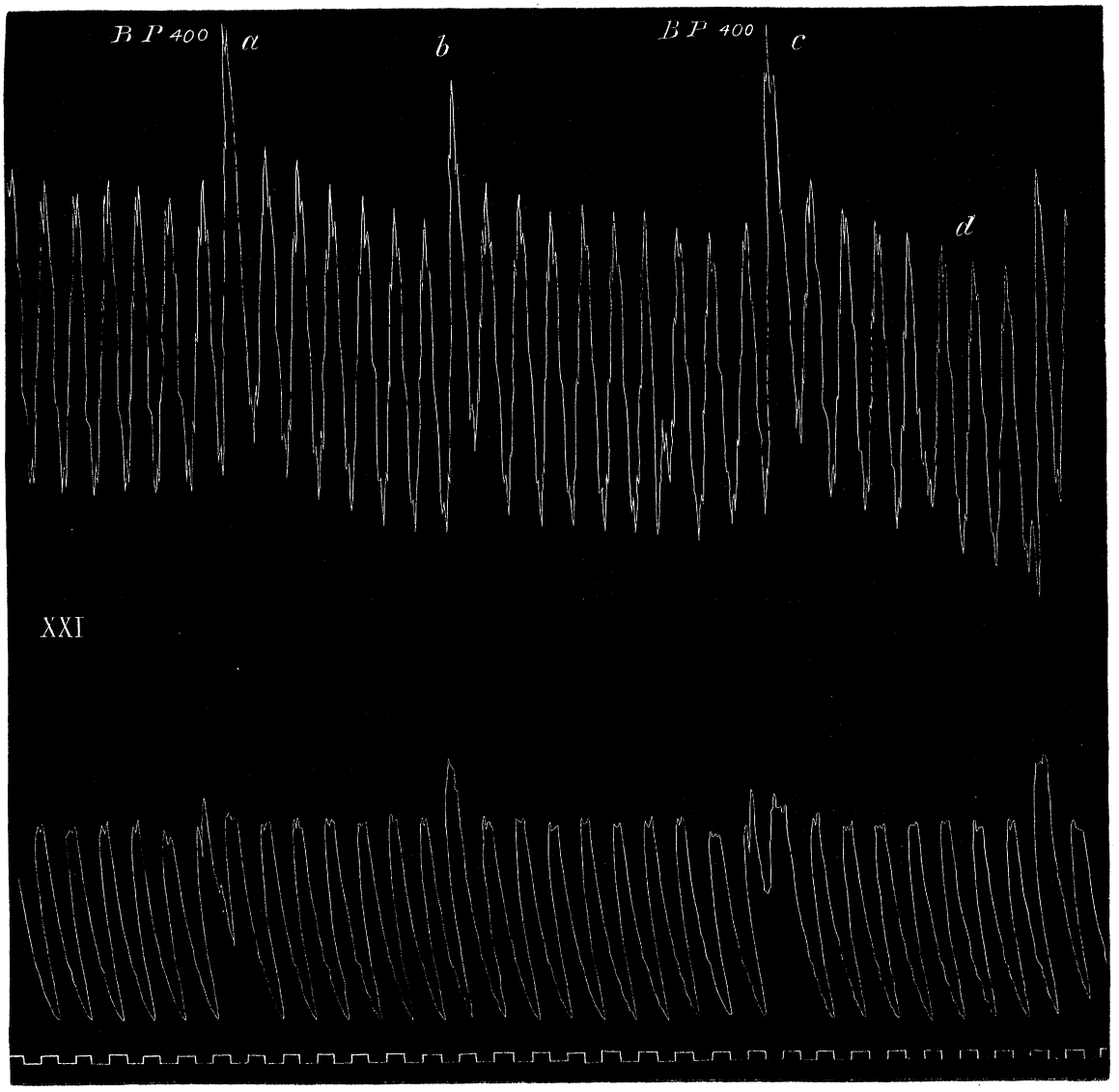
This point may be even as high as 300 mm. Hg, *i.e.*, about twice the blood pressure of a large normal Dog.

A still further rise of the blood pressure can be produced by starting artificial respiration, and so improving the condition of the vasomotor centres. (See Tracing XX.)

Finally, an extremely high blood pressure, *e.g.*, actually 400 mm. Hg, can be obtained in the following manner :—

The vagi having been divided while the blood pressure is good (*i.e.*, 130 mm. Hg), and the intra-cranial pressure raised, but not so severely as to arrest respiration, the blood pressure will, in accordance with what has just been said, be found to have risen to nearly 300 mm. Hg. If now artificial respiration be commenced and the

Tracing XXI.



The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, the lower that of the Time.

intra-cranial pressure increased, it will be found that the blood pressure will continue to rise to about 340–360 mm., and then while at this great height it will rise to even 400 mm. if a natural inspiratory impulse happen to coincide with the commencement of an artificial expiration. (See Tracing XXI.)

As the vasomotor centre begins to fail under the continued pressure, this effect begins to fall off and finally disappears.

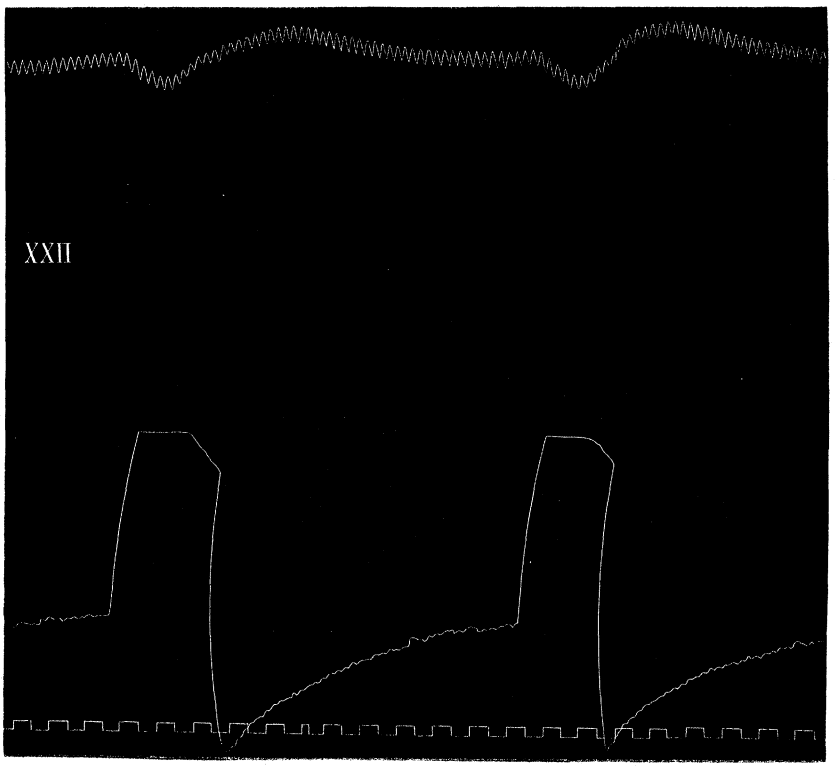
Lastly, we have already mentioned that in cases where long continued pressure has gradually caused paralysis of the vagal centres (loss of slowing), so that the heart commences to run at a rapid rate, subsequent section of the vagi has no effect on the already high blood pressure.

A. (3). R. The effect on respiration; the vagi being divided.

The effect on the respiratory movements of raising the intra-cranial pressure under these circumstances is almost always to produce an increase of movement, as follows:—

(1.) The vagal type of respiration may become enormously exaggerated, the pauses greatly drawn out and the movements forcible. (Tracing XXII.)

Tracing XXII.



The upper line is the tracing of the Blood-pressure, the middle that of the Respiration the lower that of the Time.

(2.) The division of the vagus when the pressure has already arrested respiration may furnish an inspiratory stimulus of complete adequacy, so that the respiratory movements recommence and continue. (See Tracing XIX.) This is no doubt due to the coincident rise of blood-pressure.

(3.) Occasionally an inspiratory spasm may be evoked at the moment of putting on the pressure.

Frequently acceleration of the rate of respiration was noted shortly before arrest occurred.

Division B.—*Examination of the Results obtained by directly raising the pressure in the fourth ventricle.*

As this forms a special division of the present research, we have postponed detailing the method of experiment until now.

The occipito-atlantal membrane and part of the occipital bone having been removed, a small olive-shaped bag, measuring when collapsed only 0·5 c.c., was inserted gently into the fourth ventricle by means of a probe, the direction taken being rather towards the raised up cerebellum, so as to avoid pressure on the floor of the ventricle. The bag was found to effect local distension of the ventricle, exactly according to the depth it was inserted.

By such direct pressure it was hoped that differentiation of the effects described in Division A might be obtained, and to a certain extent this succeeded.

The three "centres," analysis of which was desired, were of course:—

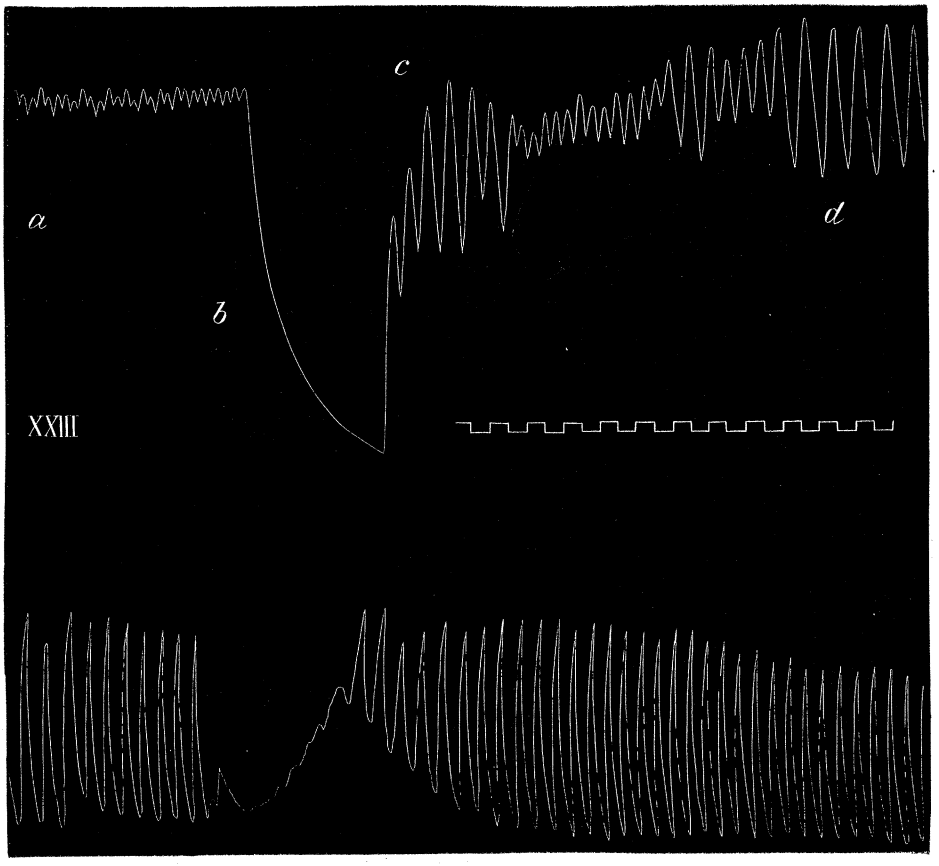
(1.) The Respiratory.
(2.) The Vasomotor.
(3.) The Cardio-Inhibitory.

It goes without saying that the modes in which these centres were first excited and then paralysed resembled in every way those we have previously considered, so that the points we wish to emphasise now relate to the interaction of these centres more than the absolute changes in their functions. The results may consequently best be grouped in the following manner:—

(*a*.) Affection of the respiratory centre without change in the cardio-inhibitory apparatus.
(*b*.) Affection of the cardio-inhibitory apparatus without alteration of respiration.
(*c*.) Concomitant paralysis of the three centres.

(*a*.) The respiratory, we have seen before, is of all the bulbar mechanisms the most sensitive. While, however, as will be seen in Tracing XXIII., if the pressure be applied to the region of the calamus, both the heart's action and respiration are simultaneously arrested, the respiratory function can be gravely altered alone if the centre of pressure be shifted lower, so as to principally act upon the first segment of the spinal cord.

Tracing XXIII.

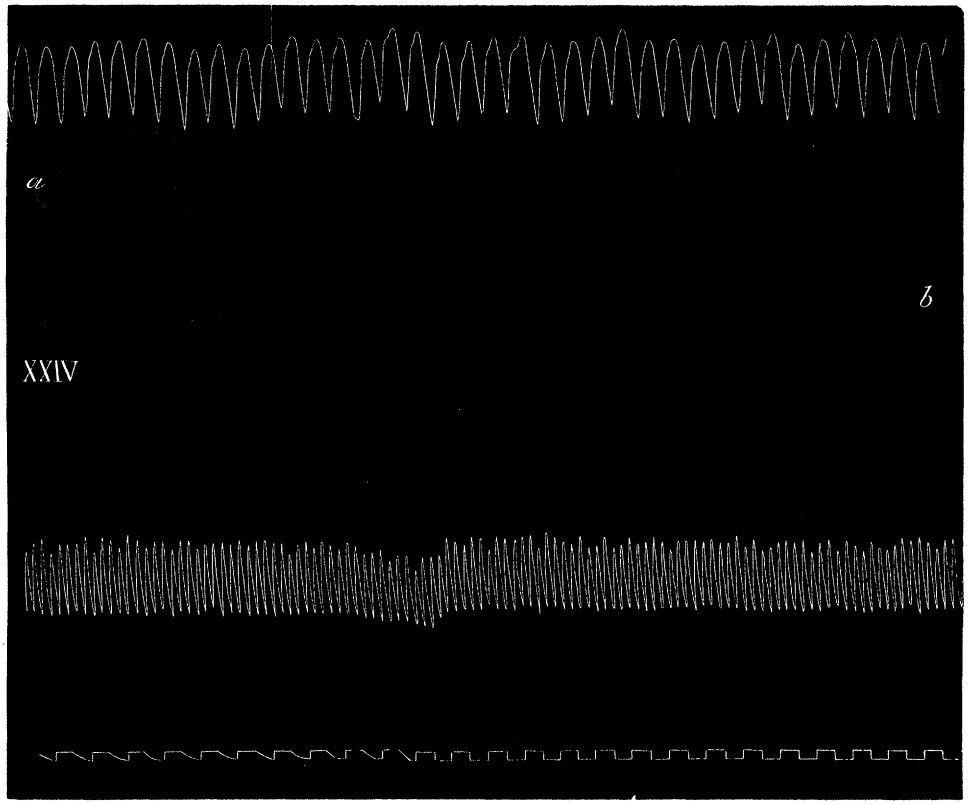


The upper line is the tracing of the Blood-pressure, the middle that of the Time, the lower that of the Respiration.

(*b.*) That the cardio-inhibitory apparatus can be excited without concomitant excitation (or paralysis) of the respiratory centre is shewn by Tracing XXIV., in which, after the pressure had been first applied to the upper part of the fourth ventricle, and then taken off, the heart's rate continued to be slow, and the systole prolonged, while the respiration went on at a rapid rate, almost three times that of the heart.

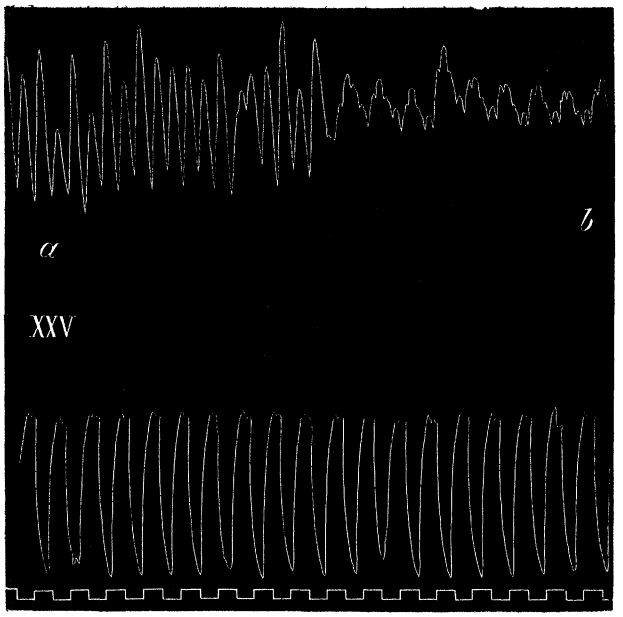
(*c.*) Paralysis of all three centres is well exemplified in Tracing XXV., where is seen the slow rate of the heart giving place to rapidity as the vagal centre loses its inhibitory influence; and, further, the respiratory centre having failed completely, artificial respiration is perforce employed. In the same tracing there is seen to be an absence of the usual pressor effect consequent upon paralysis of the vagal centre. Consequently, the vasomotor centre must be in part abrogated. That it was not wholly so was seen by the effect of asphyxia, but at least it was impaired. The centre of the pressure under these circumstances was in the middle of the ventricle.

Tracing XXIV.



The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, the lower that of the Time.

Tracing XXV.



The upper line is the tracing of the Blood-pressure, the middle that of the Respiration, the lower that of the Time.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

6. *Summary of Results.*

We have, therefore, by means of an increase in intra-cranial pressure caused decrease and alteration of functional activity, partial or complete, of three "centres" existing in the medulla. The effect of the pressure has been both excitatory and paralytic, according to its degree, and the series of events followed one another in a definite order. We will summarise the facts observed under the headings we have already employed.

The Heart.—Slight pressure reduced the rapid heart-beat of the Dog to 130 or so per minute in the same way as deep etherisation. Intermissions of the heart-beat sometimes occurred before any marked slowing. With further pressure the heart was slowed and arrested. The immediate removal of the pressure after arrest of the heart, or at most before the expiration of 10 or 20 seconds, allowed the heart to start again, but unlike the electrical stimulation of the vagus nerve, the arrest of the heart continued unless the pressure was removed. Artificial respiration cannot prevent the heart from being arrested, although a more severe pressure may be required to effect this than when artificial respiration is not in use. However, this power of arresting the heart is quickly weakened, and the heart starts again, whilst that pressure remains which just before arrested it, provided that the artificial respiration is continued.

After the removal of pressure, the slowing of the heart usually continued for some short time, and did not cease immediately; there being a gradual return to the normal.

When the pressure was continued, and artificial respiration at the same time kept up, the heart continued slow, and then gradually returned to its normal rate, as if the pressure had become compensated, and as if the cardio-inhibitory apparatus ceased to be stimulated. But with more severe pressure the change was different; the slow heart, after a period, quickened rapidly until it reached the rate which follows division of the vagi. This points to a complete paralysis of the cardio-inhibitory apparatus; but if the pressure were then taken off, and a pause made, it was found that the cardio-inhibition recovered, and that the heart could be slowed or even arrested again by pressure. But the paralysis of this cardio-inhibitory apparatus was more easily obtained on the second application of pressure.

The Blood Pressure.—The vasomotor "centre" was also at first stimulated, then partly stimulated, partly paralysed, and finally completely paralysed. With increased intra-cranial tension insufficient to slow the heart, the normal vasomotor curves were rendered more prominent, and the rhythmic character slowed, so that the curves appeared longer. With a rapid rise of intra-cranial tension there was only a slight rise (*i.e.*, excitation effect) of blood pressure in the Dog; but in the Monkey pressor influences at this stage were better marked. Depressor influence may be excited without any previous rise of blood pressure, and the blood pressure may fall greatly

before the heart is arrested; also it may persist after the heart has begun again, and only slowly disappear even when the vagi are divided. But this depressor influence is easily lost, so that on repeating the experiment a fall of blood pressure does not take place, nor can the heart be arrested, although it may be greatly slowed. When under this condition, the blood pressure may be about the normal level; but a further rise of intra-cranial tension may still further stimulate pressor influences, so that the blood pressure may rise to the level reached after division of the vagi, as shown by the absence of any further rise when this operation is performed. When the intra-cranial tension is relieved, the blood pressure returns to a level generally a little higher than normal, *i.e.*, when no depressor influences can be called forth.

With long-continued and severe pressure, and in spite of the continuation of artificial respiration, the pressor influences were lost, and the vasomotor tone was gradually reduced until the blood pressure fell to 30 mm. Hg, *i.e.*, to about the level observed after division of the spinal cord below the medulla.

When both vagi are divided there is of course normally a rise of blood pressure. If depressor influences be active at the time the rise is only gradual, but when depressor influences have been lost, or are not active, the rise is as rapid as when there is no increased intra-cranial tension. The height reached when the vagi are divided whilst the intra-cranial tension is raised is much greater. But the actual amount of rise as before mentioned is dependent for its extreme development upon the pre-existent activity of pressor influences. The blood pressure may have been so raised in this manner that no further rise takes place on division of the vagi.

After division of the vagi the blood pressure can be raised higher still by the employment of artificial respiration, and by increase of the intra-cranial tension. Phenomenally high blood pressure we have thus produced, if at the stage just described attempts at natural respiration should occur during the artificial respirations. Nevertheless, the vasomotor tone is gradually paralysed (just the same as when the vagi are not divided) with a consequent fall of blood pressure, since at this low level 30 to 60 mm. Hg, there is no effect produced when severe intra-cranial pressure is applied, the only result in fact being to still further lower vasomotor tone. And this vasomotor tone, once lost, is not recovered from.

The Respiration.—The uncertainty with regard to first principles concerning the action of the respiratory "centre" greatly hinders the distinction of the different stages of its disturbance by increase of the intra-cranial pressure. Still we believe that an excitatory and paralysing result respectively may be observed, although the various phenomena are not so clear as in the case of the heart. The excitatory effect appears to be evidenced by the inspiratory spasms we have often observed. The paralytic effect was shown to appear gradually by diminished extent of each movement, by slowing of the rhythm, and finally by arrest. Artificial respiration quickly removed the paralytic effect, and after cessation of the former a stage of apnœa occurred, followed by regular respirations. When more severe pressure was

used the apnœa did not appear, but after a relatively longer application of pressure respiration began immediately after the cessation of artificial aëration but with diminished extent. We did not obtain acceleration of respiration from increased intra-cranial pressure when etherisation was complete, except after division of the vagi.

We must now summarise the relations of the heart rate, the blood pressure and respiration to one another, when the intra-cranial pressure was increased.

If depressor influences were active and had not been impaired in any way, then the slowing of the respiration was accompanied by slowing of the heart and a fall of blood pressure. When the respiration was arrested the heart was greatly slowed, and then stopped. But if the depressor influence had been lost the heart was only slowed a little on the arrest of respiration, and there was no fall of blood pressure nor arrest of the heart, and the slight slowing was altogether lost when the heart was acting very quickly consequent upon paralysis of the cardio-inhibitory apparatus. The blood pressure affected the heart rate apart from any cardio-inhibitory effect, for after division of the vagi the heart became quickened as the blood pressure rose, and slowed as it fell.

Respiration was directly influenced by the blood pressure, as shown by the fact that a rise of blood pressure, the intra-cranial pressure remaining as before, tended to start respiration again. Respiration began again, moreover, after artificial respiration had been kept up a sufficiently long time for pressor influences to be established, although the intra-cranial pressure still remained at the height which had arrested the respiratory movements just before when the blood pressure was lower. And conversely, no regular respiration could be obtained with low blood pressure, owing to loss of the vasomotor tone. After division of the vagi under which circumstance a sudden increase of intra-cranial pressure caused a marked rise of blood pressure, we were able to excite respiration again by rapidly increasing the intra-cranial pressure, owing to its influence in further raising the blood pressure.

After division of the vagi, and after commencement of artificial respiration, if the intra-cranial pressure were increased beyond what had sufficed to stop the natural respirations until the blood pressure was raised from 320 to 360 mm. Hg, then natural respirations occurred amongst the artificial ones, and they reacted on the vasomotor centre producing the phenomenally high pressure before mentioned. We were able often to foretell that respiration was just about to begin by noticing a rise of blood pressure.

Artificial respiration had great influence in raising the blood pressure until vasomotor tone was abolished, then its efficacy was lost.

By means of our further experiments directly upon the fourth ventricle we have shown that respiration is arrested alone without slowing of the heart when the upper end of the spinal cord is pressed upon immediately below the calamus, although the blood pressure may naturally fall if the compression be severe. When respiration is

slowed or arrested along with slowing or arrest of the heart, and a fall of blood pressure is simultaneously produced, it is the lower portion of the floor of the fourth ventricle which is pressed upon.

In the upper part of the fourth ventricle the heart may be slowed, and the blood pressure rise, without respiration being hindered in the least, or it may be even accelerated.

Between these two points respiration is arrested and the heart slowed, while the blood pressure may fall slightly at first, but this fall is quickly changed into a rise above the normal.

In a paper to follow this one, one of us will consider the results of electric excitation of the floor of the fourth ventricle, and we believe that we shall be able to show an exact agreement between the results obtained by the two methods of experiment, viz., pressure and excitation.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

TABULAR Description of Tracings (the small letters correspond to those on the tracings.)

	Rate of paper cm. per minute.	Pressure in rubber bag mm. Hg.	Cranial content less in c.c.	Blood pressure mm. Hg.	Heart rate per minute.	Rate of respiration per minute and Character of respiration.
TRACING I. EXPERIMENT D.* 43. *Intermissions in the Heart Beats.*						
Pressure applied over the frontal lobe, between bone and dura mater.						
Before the experiment	7	..	..	130 to 122	130	95. Normal
a. Application of pressure	7	100	..	110 ,, 102	140	130. ,,
b. 40 seconds after *a*	7	100	1	122 ,, 116	140	130. ,,
NOTE.—The rise above the average level is due to the recoil of the mercury.						
TRACING II. EXPERIMENT D. 71. *Abnormal Respiratory Variations in Blood Pressure.*						
Pressure applied in the substance of the frontal lobe.						
Before the experiment	14·5	..	..	150 ,, 142	175	90. ,,
a. 2 minutes after the application of pressure	14·5	250	6	142 ,, 137	170	70. Deep inspirations at intervals
b. 3 ,, ,, ,,	14·5	250	7	142 ,, 132	120	25. Pause longer, with inspirations of varying depth
c. 4 ,, ,, ,,	14·5	250	7·2	142 ,, 135	110	9. Pause longer, with inspirations of varying depth
TRACING III. EXPERIMENT D. 60. *Vasomotor Curves Appearing and Growing Longer with Increasing Force.*						
Pressure applied over the cerebellum, between the bone and dura mater.						
Before the experiment	14·5	..	..	130 ,, 114	110	80. Normal
a. Application of more pressure	14·5	500	2·4	132 ,, 102	105	80. ,,
b. 30 seconds after *a*	14·5	500	3	140 ,, 110	90	75. ,,
c. Application of more pressure.						
d. 1 minute after *c*	14·5	550	3·2	130 ,, 110	110	80. ,,
e. Application of more pressure	14·5	600	3·2	140 ,, 110	90	85. ,,

* The letter D or M after the word experiment indicates the nature of the animal, *i.e.*, whether Dog or Monkey. The number immediately following is the number of the animal in the series employed.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

TABULAR Description of Tracings—(continued).

	Rate of paper cm. per minute.	Pressure in rubber bag mm. Hg.	Cranial content less in c c.	Blood pressure mm. Hg.	Heart rate per minute.	Rate of respiration per minute and Character of respiration.
TRACING IV. EXPERIMENT D. 96.						
Slight Primary Rise of Blood Pressure.						
Pressure applied anterior to frontal lobe between the dura mater and brain.						
Before the experiment	14·5	..	..	160 to 148	130	90. Normal
a. Application of pressure	14·5	300	..	145 ,, 135	150	90. ,,
b. 30 seconds after *a*	14·5	300	6	160 ,, 151	150	85. ,,
TRACING V. EXPERIMENT M. 43.						
1*st Part.* *Primary Rise of Blood Pressure in the Monkey.*						
Pressure applied over the occipital lobe between the bone and dura mater.						
Before the experiment	14·5	..	..	80 ,, 72	160	37. Normal
a. Application of more pressure	14·5	500	5·1	85 ,, 77	160	35. ,,
b. 10 seconds after *a*	14·5	500	6	99 ,, 93	160	40. ,,
c. 20 seconds after *a*	14·5	500	6·8	140 ,, 130	140	Inspiratory spasm
d. 24 seconds after *a*	14·5	500	7	120 ,, 100	95	Arrested
e. Pressure removed						
f. 10 seconds after *e*	14·5	..	..	100 ,, 80	90	Arrested
g. 40 seconds after *e*	14·5	..	..	110 ,, 100	150	30
TRACING VI. EXPERIMENT M. 43.						
Loss of the Primary Rise.						
Pressure applied as in Tracing V.						
h. Application of pressure	14·5	500	..	90 ,, 84	130	57. Normal
i. 10 seconds after *h*	14·5	500	5	66 ,, 60	70	20. Shallow, irregular

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Tabular Description of Tracings—(continued)

	Rate of paper cm. per minute.	Pressure in rubber bag mm. Hg.	Cranial content less in c.c.	Blood pressure mm. Hg.	Heart rate per minute.	Rate of respiration per minute and Character of respiration.
Tracing VII. Experiment D. 64.						
Depressor Effect Well Marked, Persisting after Division of Vagi.						
Pressure applied over cerebellum between dura mater and brain.						
Before the experiment	14·5	..	..	150 to 142	150	60. Normal
a. More pressure applied	14·5	500	3·2	148 ,, 136	130	50. ,,
b. 10 seconds after *a*	14·5	500	3·5	128 ,, 120	120	60. ,,
c. 20 seconds after *a*	14·5	500	4	104 ,, 92	120	70. Very shallow
d. 30 seconds after *a*	14·5	500	4	86	80	Arrested
e. 40 to 45 seconds after *a*, division of both vagi						
f. 1 minute after *a*, 15 seconds after division of vagi	14·5	500	4·5	82 ,, 70	120	,,
g. 1½ minute after *a*, 30 seconds after division of vagi	14·5	500	5·4	106 ,, 94	130	,,
In 3 minutes after *a*, the blood pressure had risen to 190 mm. Hg.						
Tracing VIII. Experiment D. 96, Continuation of Tracing IV.						
Slowing and Arrest of Heart and Respiration; the Recovery of the Heart Immediately on Starting Artificial Respiration.						
Pressure as in Tracing IV.						
c. 1 minute after application of pressure	14·5	300	6·3	153 to 133	110	60. Shallow
d. 1½ minute ,, ,,	14·5	300	6·4	139 ,, 87	70	Arrested
e. 1 minute 42 seconds after application of pressure	14·5	300	6·6	Zero	Arrested	,,
f. 1 minute 54 seconds after application of pressure, artificial respiration started	14·5	300	6·8	Immediate rise	?	24. Artificial
g. 2 minutes 20 seconds after application of pressure	14·5	300	7	143 to 125	115	24. ,,

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

TABULAR Description of Tracings—(continued).

	Rate of paper cm. per minute.	Pressure in rubber bag mm. Hg.	Cranial content less in c.c.	Blood pressure mm. Hg.	Heart rate per minute.	Rate of respiration per minute and Character of respiration.
TRACING IX. EXPERIMENT D. 96.						
Arrest of the Slowed Heart after Removal of the Pressure, on Account of the Absence of Respiration.						
Pressure applied anterior to the frontal lobe, between the bone and dura mater.						
Before the experiment	14·5	..	..	160 to 144	130	95. Normal
a. 30 seconds after the application of more pressure	14·5	400	5	142 „ 122	100	95. „
b. 44 seconds after the application, all pressure removed	14·5	..	..	146 „ 100	70	Arrested
c. 4 seconds after *b*	14·5	..	..	Zero	Arrested	„
d. 12 seconds after *c* artificial respiration begun						
e. 30 seconds after *d*	14·5	..	..	110 to 90	80	24. Artificial
TRACING X. EXPERIMENT D. 81.						
The Heart Re-starting after Arrest, but Continuing Slow.						
Pressure applied in the fourth ventricle.						
Before the experiment	14·5	..	..	115 to 95	90	30. Normal
a. Application of more pressure	14·5	100	1·5	132 „ 76	50	50. Irregular
b. 12 seconds after *a*	14·5	100	1·5	Zero	Arrested	50.
c. 12 seconds after *b*	14·5	100	1·5	„	„	Arrested.
d. 16 seconds after *c*, artificial respiration begun						
e. 40 seconds after *d*	14·5	100	1·8	145 to 95	35	34. Artificial
TRACING XI. EXPERIMENT D. 96.						
Arrest of Heart during Artificial Respiration, its Recovery, and the Appearance of Respiratory Variations in Blood Pressure.						
Pressure applied anterior to the frontal lobe, between the dura mater and the brain.						
Before the experiment	14·5	..	..	160 to 144	130	95. Normal
a. 40 seconds after application of more pressure	14·5	400	8	121 „ 41	65	24. Artificial
b. 42 „ „ „	14·5	400	8	Zero	Arrested	24. „

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

TABULAR Description of Tracings—(continued).

	Rate of paper cm. per minute.	Pressure in rubber bag mm. Hg.	Cranial content less in c.c.	Blood pressure mm. Hg.	Heart rate per minute.	Rate of respiration per minute and Character of respiration.
c. 1 minute after application of more pressure, pressure removed	14·5	..	..	Zero	Arrested	24. Artificial
d. 40 seconds after *c*	14·5	..	..	,,	,,	24. ,,
e. After a pause the heart started	14·5	..	..	130 to 58	50	24. ,,
f. After another pause, artificial respiration was stopped	14·5	..	..	162 ,, 102	80	
Natural respiration began						
g. 1 minute after natural respiration had begun	14·5	..	..	170 ,, 122	90	18. Deep with long pauses
TRACING XII. EXPERIMENT 96.						
Arrest of the Heart, Starting again by Forcible Beats, Separated by Long Intervals.						
Pressure applied as in Tracing XI., after recovery.						
a. 40 seconds after application of pressure again	14·5	300	7	152 ,, 134	100	55. Normal
b. 1 minute after ,, ,,	14·5	300	7	Zero	Arrested	Arrested
c. 1 minute 22 seconds after application of pressure again	14·5	300	7	,,	,,	23. Artificial
After a pause, with artificial respiration continued, and re-starting of heart and rise of blood pressure						
d. 3 minutes after application of pressure	14·5	300	7·5	214 to 114	30	23. ,,
TRACING XIII. EXPERIMENT D. 95.						
Increased Rapidity of the Heart after Slowing as great as the Rate which follows Division of the Vagi.						
Pressure applied anterior to the frontal lobe between the bone and dura mater.						
Before the experiment	14·5	..	..	120 to 106	125	115. Normal
a. Application of more pressure	14·5	500	..	150 ,, 100	85	25. Artificial
b. About 1 minute after *a*	14·5	500	..	260 ,, 256	220	25. ,,
c. Pressure removed						
d. About 1 minute after *c*	14·5	..	..	115 ,, 65	80	40. Short inspirations

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

TABULAR Description of Tracings—(continued).

	Rate of paper cm. per minute.	Pressure in rubber bag mm. Hg.	Cranial content less in c.c.	Blood pressure mm. Hg.	Heart rate per minute.	Rate of respiration per minute and Character of respiration.
TRACING XIV. EXPERIMENT D. 72.						
Rapidity of Heart Rate uninfluenced by Division of the Vagi.						
Pressure applied in the substance of the occipital lobe.						
Before the experiment	10	..	..	130 to 125	150	85. Normal
a. Application of more pressure	10	400	..	244 ,, 240	210	36. Artificial
b. 1 minute after *a*, both vagi divided	10	400	..	260 ,, 256	200	36. ,,
c. 12 seconds after *b*	10	400	..	260 ,, 256	190	36. ,,
TRACING XV. EXPERIMENT D. 91.						
Fall of Blood Pressure preceding the Slowing of the Heart, and continuing after Recovery of the Rhythmic Heart Rate.						
Pressure applied anterior to the frontal lobe between the skull and dura mater.						
Before the experiment	14·5	..	..	100 to 90	110	85. Normal
a. 30 seconds after the application of pressure	14·5	300	5·5	130 ,, 122	110	60. ,,
b. 1 minute after application of pressure	14·5	300	6	Zero	Arrested	Arrested
c. 2 minutes after application of pressure, and 1 minute after *b*	14·5	300	6·5	75 to 55	120	38. Artificial
TRACING XVI. EXPERIMENT D. 69.						
Depressor Influences absent, although the Pressure was applied for the first time, and also absent after the Arrest of Respiration.						
Pressure applied in the substance of the frontal lobe.						
Before the experiment	14·5	..	..	130 to 120	140	68. Normal
a. Application of pressure	14·5	300	..	52 ,, 40	95	90.
b. 34 seconds after *a*	14·5	325	4	68 ,, 50	85	70.
c. 20 seconds after *b*	14·5	350	5	72 ,, 46	75	55.
d. 42 seconds after *c*	14·5	350	7	80 ,, 44	48	Arrested
e. Pressure removed						
f. 10 seconds after *e*	14·5	..	..	68 ,, 32	35	Arrested
g. Artificial respiration started						
h. Natural respiration began						

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

TABULAR Description of Tracings—(continued).

	Rate of paper cm. per minute.	Pressure in rubber bag mm. Hg.	Cranial content less in c.c.	Blood pressure mm. Hg.	Heart rate per minute.	Rate of respiration per minute and Character of respiration.
TRACING XVII. EXPERIMENT D. 91.						
Depressor Effect absent when Pressure was applied for the Second Time.						
Pressure anterior to frontal lobe between the dura mater and the brain.						
Before second experiment	14·5	..	..	134 to 126	105	55. Normal
a. 30 seconds after the application of pressure	14·5	300	5·8	160 „ 148	105	40. Pauses longer
b. 1 minute 6 seconds after „	14·5	300	6·5	150 „ 136	95	Arrested
c. 18 seconds after *b*	14·5	300	7	150 „ 136	90	„
TRACING XVIII. EXPERIMENT D. 43.						
Pressor Influences causing a marked Rise in Blood Pressure, while the Heart was much Slowed.						
Pressure applied over the cerebellum between the dura mater and the brain.						
Before the experiment	7	..	..	130 „ 122	130	95. Normal
a. Application of pressure	7	100	..	100 „ 96	170	
b. 15 seconds after *a*	7	200	2	110 „ 64	40	
c. 40 seconds after *b*	7	200	4	205 „ 150	40	
TRACING XIX. EXPERIMENT D. 56.						
Division of the Vagi releasing the Heart and Respiration from Arrest.						
Pressure applied over the frontal lobe between the dura mater and brain.						
Before the experiment	14·5	..	..	140 „ 120	120	100. Normal
a. 9 seconds after application of pressure	14·5	350	6	128 „ 108	130	140
b. 24 „ „ „	14·5	350	7	132 „ 102	100	Arrested
c. 28 „ „ „	14·5	350	7	Zero	Arrested	Arrested
d. 30 to 34 „ „ „	14·5	350	7	Rise	?	Inspiratory spasm
e. 30 seconds after *d*	14·5	350	8	188 to 178	190	40. Deep

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

TABULAR Description of Tracings—(continued).

	Rate of paper cm. per minute.	Pressure in rubber bag mm. Hg.	Cranial content less in c.c.	Blood pressure, mm. Hg.	Heart rate per minute.	Rate of respiration per minute and Character of respiration.
TRACING XX. EXPERIMENT D. 60.						
Further Rise of Blood Pressure on starting Artificial Respiration, the Vagi having been Divided, and sufficient Pressure to stop Natural Respiration employed.						
Pressure applied over the cerebellum, between the bone and dura mater.						
a. Artificial respiration begun	14·5	600	5	180 to 162	150	36. Artificial
b. 20 seconds after *a*	14·5	600	5·2	280	?	36. „
TRACING XXI. EXPERIMENT D. 62.						
Very High Blood Pressure after Division of Vagi.						
Pressure over occipital lobe, between bone and dura mater.						
a. 2 minutes 20 seconds after application of pressure	14·5	400	6	400	?	33. Artificial, with natural respiration
b. 10 seconds after *a*	14·5	400	6	378	?	33. Artificial, with natural respiration
c. 20 „ „ *b*	14·5	400	6	400	?	33. Artificial, with natural respiration
d. 10 „ „ *c*	14·5	400	6	326	?	33. Artificial only
TRACING XXII. EXPERIMENT D. 74.						
Enormously Exaggerated Respirations of Vagal Type.						
Pressure applied in the substance of the temporo-sphenoidal lobe.						
Division of vagi and application of pressure . .	14·5	..	..	135 to 130	140	2. Inspiration; length, 4·5 seconds.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

TABULAR Description of Tracings—(continued).

	Rate of paper cm. per minute.	Pressure in rubber bag mm. Hg.	Cranial content less in c.c.	Blood pressure mm. Hg.	Heart rate per minute	Rate of respiration per minute and Character of respiration.
TRACING XXIII. EXPERIMENT D. 82.						
Instantaneous Arrest of Heart and Respiration on Application of Pressure.						
Pressure applied in the fourth ventricle.						
a. Before the experiment	14·5	..	..	115 to 112	120	46. Normal deep
b. Application of pressure	14·5	50	..	Zero	Arrested	Arrested
c. Bag pushed further into fourth ventricle						
d. 26 seconds after *c*	14·5	50	0·6	135 to 93	40	65. Deep
TRACING XXIV. EXPERIMENT D. 79.						
Slowed Heart with Prolonged Systole, whilst Respiration was Rapid.						
Pressure applied in the fourth ventricle.						
After removal of pressure	14·5	..	..	106 „ 86	45	125. Normal
					43	130. „
TRACING XXV. EXPERIMENT D. 75.						
Paralysis of Cardio-inhibitory, Vasomotor, and Respiratory Centres.						
Pressure applied in the fourth ventricle.						
Before the experiment	14·5	..	..	100 „ 98	?	50. „
a. After pressure had arrested respiration, abolished pressor influences, and slowed the heart	14·5	300	6	90 „ 50	65	35. Artificial
b. 30 seconds after	14·5	300	6	80 „ 78	140	35. „
More pressure was applied, and the blood pressure fell to 50 mm. Hg						
The vagi were then divided without causing any change						