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Hering and Breuer[1] in 1868 first described an apnoea resulting from distension of the lungs. They produced the phenomenon in dogs by closing the trachea at the height of a normal or artificially increased inspiration. By the use of air containing little or no oxygen they further showed that the apnoea was not due to an excess of oxygen. They were unable, however, to obtain an apnoea by the same procedure after section of the vagi. They concluded, therefore, that the pause was a result of inspiratory inhibition due to the excitation of the vagi by stretching the lungs.

Their experimental results were duplicated by many observers and the phenomenon has become generally spoken of as the Hering-Breuer inhibitory effect.

Head[2] in 1889 reported from Hering's laboratory a very extensive study on the effect of distension and other forms of natural stimuli on the respiratory mechanism. At that time, however, it was not known that the respiratory centre was extremely sensitive to changes in the carbon dioxide tension of the arterial blood[3] and, therefore, many of the experimental results were

[1] Hering and Breuer: Die Selbsteuerung der Athmung durch den Nervus Vagus. Sitzgsber. d. Wiener Acad., Math.-natur., 1868, lvii, 672; lviii, 909.

[2] Head: On the regulation of respiration. Jour. Phys., 1889, x, 1–70; 279–290.

[3] Haldane and Priestly: The regulation of the lung ventilation. Jour. Physiol., 1905, xxxii, 225–266.

erroneously interpreted as evidence of vagal influence. On the other hand, his experiments are very accurately described and profusely illustrated by kymographic records, and the data are still of great value and capable of reinterpretation.

Haldane and Lorrain Smith[4] later showed that, in rabbits, the pause in the respiration, produced during distension of the lungs, was not due to a lowering of the alveolar carbon dioxide pressure. In consequence, this particular experiment has survived as the only example of a "natural stimulus" which produces respiratory inhibition by stretching the vagi.

Very recently Christiansen and Haldane[5] have studied the effect of distension of the lungs on the human respiration. They made use of a bag containing air and so weighted that the air was under a pressure of 6 to 8 cm. of water. The subject, breathing through a mouthpiece, could be connected, by means of a three-way tap, either to the air of the room or to the air in the bag. They invariably found that distension of the lungs caused the respirations to cease, usually for about half a minute. The pause was then broken by a deep expiration, followed by a further pause before the next expiration, and so on with increasingly shorter pauses. On turning the tap, so that the subject again breathed atmospheric air, the pauses disappeared, and the breathing returned to normal. By the use of air containing 7.3 per cent carbon dioxide and 8.2 per cent oxygen, the pause is produced just as with pure air; the pauses succeeding the first, however, diminished in length much more rapidly than when pure air was used. This pause was, therefore, not dependent on a lowering of the carbon dioxide tension of the arterial blood.

In addition to the above Hering and Breuer "inhibitory" effect, which is not dependent on chemical changes in the blood, Christiansen and Haldane were able to obtain clear evidence of an independent phenomenon by the fact that under certain conditions an increase of carbon dioxide in the alveolar air will break

[4] Haldane and Lorrain Smith: The physiological effects of air vitiated by respiration. Jour. Path. and Bact., 1892, i, 168–186.

[5] Christiansen and Haldane: The influence of distension of the lungs on human respiration. Jour. Physiol., 1914, xlviii, 4, 272-277.

through the inhibitory effect, and also that dilution of the alveolar carbon dioxide with pure air will augment the effect. They were able, therefore, to distinguish two distinct phenomena produced by distension of the lungs, the first being a so-called Hering-Breuer "inhibition," occurring with the thorax expanded, and the second being a true chemical apnoea, occurring with the thorax at the level of a normal expiration.

Throughout their paper, Christiansen and Haldane tactily accept, as an explanation of the primary pause, the Hering-Breuer theory of inspiratory inhibition from vagal excitation. That they are doubtful that this is the true explanation is evident from the following statement at the end of their paper: "Our experiments afford new confirmation to the view that true apnoea, apart from the inhibitory nervous effects produced during actual distension, or actual excitation along *certain other nerve paths* connected with the centre, is a 'chemical apnoea.' "

At the time of the appearance of Christiansen and Haldane's paper, investigations were being made in this laboratory on the influence of the vagi over the normal regulation of the gaseous metabolism, the pulmonary ventilation, and the gas exchange in the lungs.[6] As these studies failed to reveal evidence that the vagi possessed any demonstrable influence over these functions, we suspected that the apnoea following distension was likewise not due to vagal excitation.

For distending the lungs we made use of a Benedict respiration apparatus[7] and so weighted the spirometer that the air was under a pressure of 8 to 16 cm. of water. The subject sat in a chair and breathed through a wide-bore, three-way tap of which one branch led to the respiration apparatus, the second to the room air, and the third to the mouthpiece. The nose was closed with a clip. The subject at first breathed quietly for a short time

[6] Boothby and Shamoff: A study of the late effect of division of the pulmonary branches of the vagus nerve on the gaseous metabolism, gas exchange, and respiratory mechanism in dogs. This Journal, 1915, xxxvii.

[7] Benedict: Ein Universalrespirationsapparat. Deutschen Archiv. f. klinische Medizin. 1912, cvii, 157–200.

through the branch of the tap leading to the room air, and at various periods in the respiratory cycle the tap was suddenly turned, so as to connect the subject with the air under pressure in the respiration apparatus. By this means the lungs were rapidly distended with air and the intra-pulmonary pressure increased by a definite amount. The spirometer of the respiration apparatus, though weighted, was perfectly free to move in either direction, so that the response of the subject to the stimulus of lung distension would be unhampered by still further changes in the intrapulmonary pressure, produced by any respiratory movements that might occur. In experiments in which the trachea is clamped or the tap entirely closed after the distension, changes in pressure would naturally follow any respiratory movements. Movements, therefore, that might be too small to be recorded by a pneumograph or even by a slip of the diaphragm could possibly produce changes in intrapulmonary pressure that would give rise to secondary and confusing reactions.

In the case of the dogs, an air-tight mask was applied to the animal's head, according to the method described by Boothby and Shamoff.[8] The mask was connected to the three-way tap by rubber tubing of large bore. The dead space of the mask and tubing was about 150 cc., which was quite large in comparison with the tidal volume of air. The dogs lay quietly on their sides on a table and were unrestrained. They were perfectly comfortable and did not require anaesthesia.

By means of a pneumograph around the thorax, the respiratory movements were recorded qualitatively on the kymograph, both before and after the subject breathed the air under pressure. As soon as the tap was turned to the respiration apparatus a very accurate quantitative curve of the coordinated total respiratory movements was written by the recording spirometer.

In Figure I is given a typical tracing of the effect, on W. M. B., of distending the lungs by suddenly increasing the intrapulmonary pressure. The tap is turned at the end of a normal

[8] Boothby and Shamoff: A study of the late effect of division of the pulmonary branches of the vagus nerve on the gaseous metabolism, gas exchange, and respiratory mechanism in dogs. This Journal, 1915, xxxvii.

expiration, producing an exaggerated inspiration, as shown by the pneumograph curve below point *A*. The following expiration is abortive, as shown by both curves. The succeeding respirations are somewhat more rapid and slightly more irregular than when breathing under normal pressure. At *a* and *b* in this

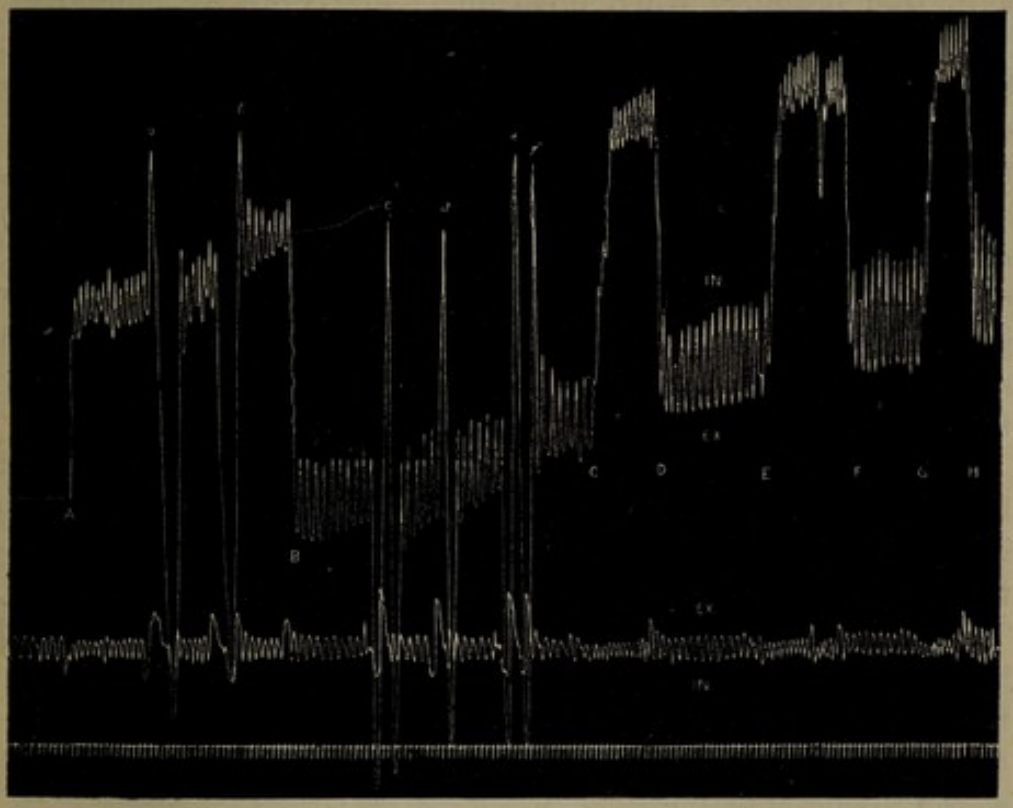

Fig. I. Effect of distension on W. M. B. Spirometer weighted to give 15 cm. water pressure. Upper curve written by the recording spirometer, with inspiration up and expiration down. Lower curve written by the pneumograph around the subject's chest with inspiration down and expiration up. To be read from left to right. At *A* tap turned so that the subject is connected with the air under pressure in the apparatus. The pneumograph shows qualitatively the preceding normal respiratory rhythm; the first effect is a total expansion of the chest, followed by faster and shallower respirations. At *a* and *b* maximum inspirations and expirations were made showing that the reserve air was greatly increased and the lungs markedly distended. At *B* the weights were removed from the spirometer and the subject then breathed air under a normal pressure. At *c*, *d*, *e*, and *f* maximum inspirations and expirations were made and are to be contrasted with those made at *a* and *b*. At *C*, *E*, and *G* the weights were replaced on the spirometer and at *D*, *F*, and *H* again removed. No evidence of apnoea either primary or secondary. Time in two seconds.

figure maximum inspirations and expirations were made, showing that the "Mittelage" is much higher than under normal conditions. At *B* the weights were removed as quickly as possible, and at *c*, *d*, *e*, and *f*, maximum inspirations and expirations were again made to contrast the "Mittelage" under normal conditions with that obtained when breathing under pressure (*a* and *b*). At *C* the weights were reapplied, but, as they consisted of five lead weights, an appreciable time was occupied in putting them on the spirometer, thus producing a less sudden increase in intrapulmonary pressure than that obtained by turning the tap, as was done at *A*. The large drop in the spirometer at *A*, *C*, *E*, and *G*, and the corresponding rise at *B*, *D*, *F* and *H* are due only in small part to the change in the "Mittelage;" the greater part is caused by the compression (expansion) of the air to a smaller (larger) volume both in the apparatus and in the lungs by the addition (removal) of the weights on the spirometer.

Figure II shows another tracing for the same subject as in Figure I. Here again, we see no inspiratory inhibition. There is, however, in this curve an irregular pause of very short duration (about three seconds), beginning in complete inspiration. This pause, excepting for its irregularity, resembles those obtained by Christiansen and Haldane on distending the lungs. The notches on both the spirometer and pneumograph curves indicate that rhythmic expiratory movements were being made but were proving abortive.

This fact can be explained on the ground that the usual stimuli coming from the respiratory centre to the muscles of respiration were not sufficiently powerful to cause those muscles to completely contract against the increased load (pressure). After a few seconds the respirations again became practically normal, as by this time the respiratory centre was sending out stimuli of sufficient strength to cause the respiratory muscles to perform the increased work thrown upon them. In experiments following each other closely the delay before normal respiration was resumed markedly decreased, and, in fact, usually entirely disappeared, as is shown in the latter part of Figure II, where the distension effect was repeated without causing apnoea.

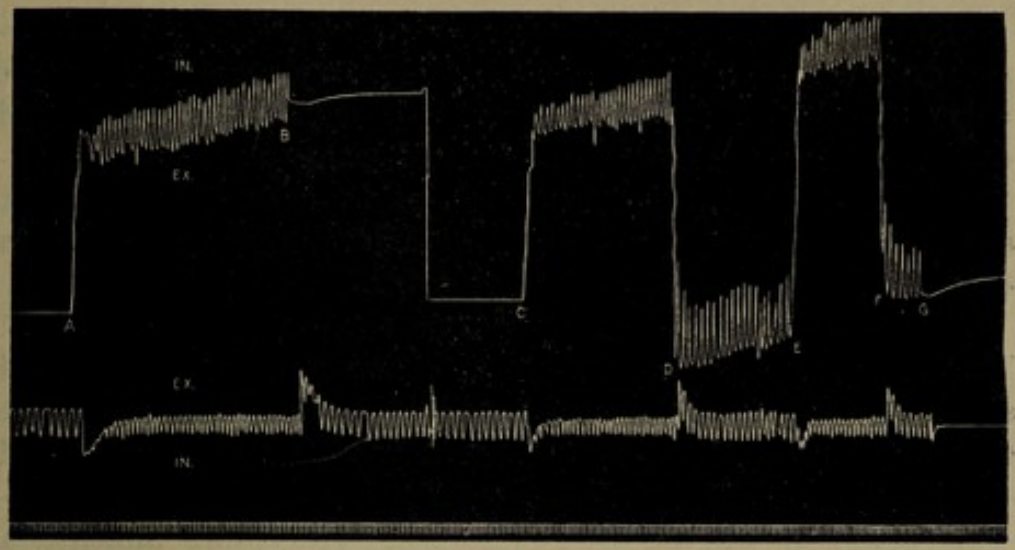

Fig. II. Effect of distension on W. M. B. Spirometer weighted to give 15 cm. water pressure. Upper curve written by the spirometer, with inspiration up. Lower curve written by the pneumograph, with inspiration down. At *A* tap turned so that the subject breathed the air under pressure in the apparatus; this was followed by rhythmical but abortive attempts at respiration. At *B* and *G* tap turned to room air. At *C* tap turned to apparatus. At *D* and *F* weights removed from the spirometer and at *E* were reapplied. No apnoea at *C* and *E*. Time in seconds.

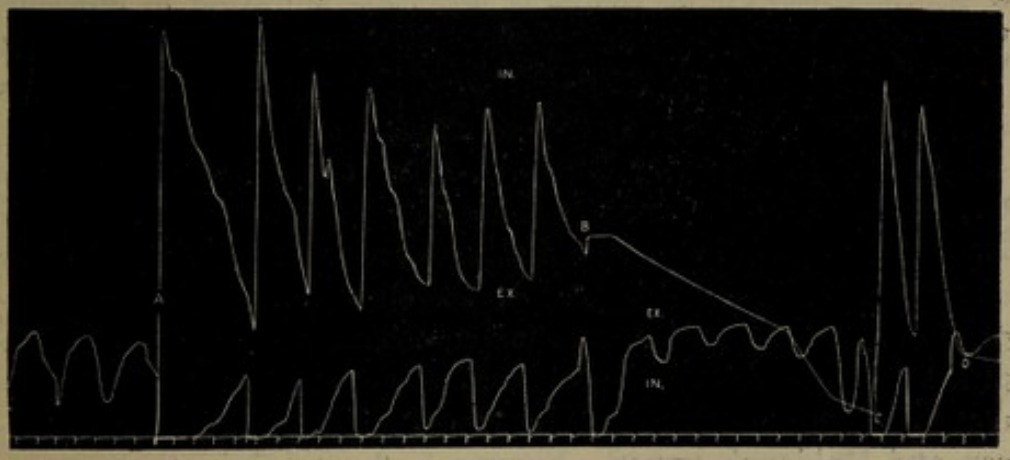

Fig. III. Effect of distension on F. B. B. Spirometer weighted to give 15 cm. water pressure. Upper curve written by the spirometer, with inspiration up. Lower curve written by the pneumograph, with inspiration down. At *A* and *C* tap turned so that the subject breathed the air under pressure. At *B* and *D* tap turned to room air. The effect of distension is first to slow and deepen the respirations, then they become faster and shallower. Inspirations are very sharp. No apnoea. Time in seconds.

The subject was careful to remain passive during every experiment and to refrain from any voluntary respiratory effort following the distension of the lungs. However, after repeated experiments, the subject appears to become somewhat accustomed to the unusual conditions and to unconsciously react more quickly to the distension. A similar adaptation occurs in the dogs, as we shall presently point out.

Figure III is a tracing obtained from another subject, F. B. B. The drum is revolving faster than in the previous figures and shows very clearly the irregularity of the first expiration. There is no delay in the commencement of the expiration but the several notches in the expiratory line indicate a somewhat irregular action or incoordination of the expiratory muscles. This curve illustrates very emphatically that there is no inhibition of inspiration in our subjects, as the next inspiration follows immediately after the completion of the expiration and is very sharp. In none of our curves nor in any of those given by Christiansen and Haldane is there any indication of a primary inspiratory inhibition. The distension apnoea in their curves is at the top of inspiration and is therefore an inhibition of expiration. The following chemical apnoea is at the bottom of expiration and shows a chemical inhibition of the respiratory movements. Figure IV is a reproduction of Figure 3 from Christiansen and Haldane's paper. Figures 5, 6, and 7 in their paper show conclusively that the secondary apnoea is chemical and not due to the same cause as the primary apnoea. The pause noted by Hering and Breuer is not at the top of inspiration but at the bottom of expiration, that is, the next expiratory phase is prolonged and inspiration is delayed, or, as they say, "inhibited" by

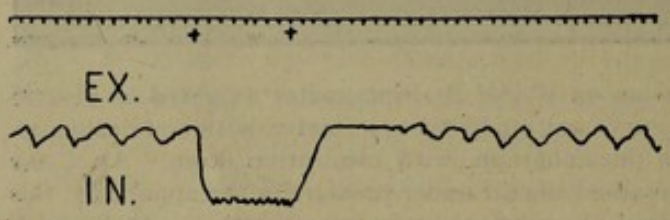

Fig. IV. Reproduction of Figure 3 from Christiansen and Haldane's paper (Jour. Physiol., xlviii, p. 274). "Effect of distension for 8 secs. Crosses show beginning and end of distension." Note the primary or distension apnoea in the position of deep inspiration and the secondary or chemical apnoea at the bottom of the normal expiration. Time in seconds.

vagal stimulation. A typical example of the Hering-Breuer phenomenon is given in Curve VI, Plate II of Head's[9] excellent paper; we reproduce this curve in Figure V.

The curves of Christiansen and Haldane at first sight appear quite different from the typical Hering-Breuer phenomenon, as shown by Head's tracing in Figure V. In the former, the primary pause is at the top of inspiration, and in the latter, at the bottom of expiration. This discrepancy, however, can be accounted for by the way in which the curves are recorded. Christiansen and Haldane used a pneumograph around the chest wall, which roughly depicted the volume of the thorax, while Head made use of a slip of the diaphragm, which represents the condition of contraction or relaxation of that muscle. The volume of the lungs could be increased passively by the air pressure with the pause apparently in the inspiratory phase, as shown by Christiansen and Haldane, and yet the diaphragm would be relaxed, as shown by Head. In our experiments, in addition to the relaxation of the diaphragm, as occurs

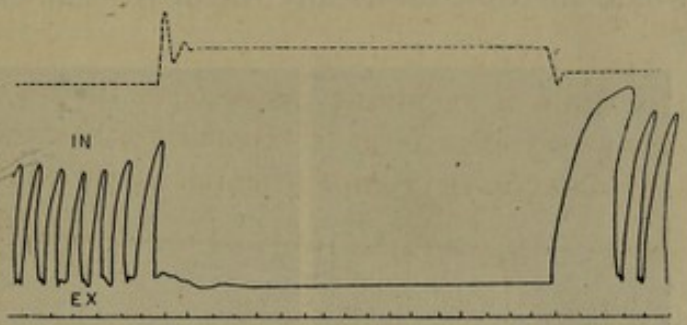

Fig. V. Reproduction of Curve VI, Plate II of Head's paper (Jour. Physiol., x). "The dotted tracing represents the movements of a mercury manometer connected with the trachea. Thus any rise on the curve represents a rise of pressure in the lungs after closure of the trachea. The respiratory curve is traced by the movements of the anterior slips of the diaphragm, separated and prepared according to the description in Head's paper, p. 4. Movement of the pointer up represents inspiration. From a rabbit weighing 1500 grams. Chloral 1¼ grams. The lungs were inflated during normal respiration and allowed to return to the normal volume before the pause had been broken by an 'interrupting' inspiration." On release of the pressure by opening the trachea, as shown by the dotted line, no movements of the diaphragm occurred until sufficient time had elapsed for the expiratory muscles to contract the thorax; then a big inspiration occured, as shown by the diaphragm reaction, followed by breathing which is deeper and slightly faster than before clamping the trachea. Time in seconds.

[9] Head: On the regulation of respiration. Jour. Phys., 1889, x, 1–70; 279–290.

probably in the experiments of Christiansen and Haldane, as well as in those of Head, there is a coincident contraction of the inspiratory group of muscles, resulting in immediate expiration without producing any pause. As the trachea was clamped in the case of Head's experiments, the air could not be expired even if the expiratory muscles contracted, and any attempt to do so would increase materially the distension effect.

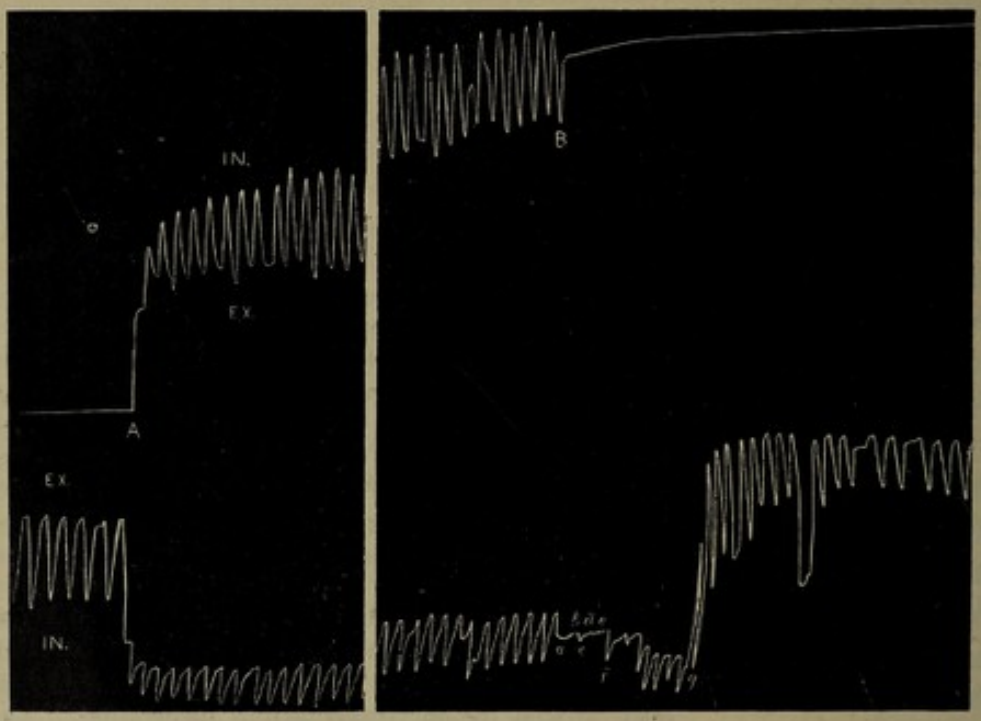

Fig. VI. Effect of distension on W. M. B. Spirometer weighted to give 15 cm. water pressure. Upper curve written by the spirometer, with inspiration up. Lower curve written by the pneumograph, with inspiration down. At *A* tap turned to apparatus. At *B* tap turned at the top of inspiration so that the air-way was entirely closed, producing the effect of clamping the trachea. The pneumograph curve shows essentially a pause lasting a considerable time; the pause, however, is broken by the notches *a*, *b*, *c*, *d*, *e*, and *f*, and finally by regular respiratory movements, although no air could go in or out of the lungs. At *g* tap was turned so that the subject could breathe normally the room air.

Figure VI is another tracing from W. M. B. At *A* the tap was suddenly turned so that the subject breathed the air under pressure in the respiration apparatus. At *B* a special tap on the

mouthpiece was closed near the end of inspiration in such a manner that the subject's air-way was entirely closed. This procedure is equivalent to clamping the trachea with the lungs distended. From the pneumograph curve, it is evident that the inspiratory movement almost instantly stopped, though probably not completely, as shown by the slight notch at *a*. The chart level then fell slightly at *b* but at *c* there is a sharp inspiratory movement. This inspiration was abortive, as no air could enter the thorax, and immediately a negative pressure was probably produced. The inspiration at *c* is slightly delayed, but the following notches *d* and *e* are very close to the normal respiratory rhythm. At *f* the subject makes a more pronounced inspiratory effort, followed by one less marked and then five which are very pronounced. The tap is then opened at *g*, so that the subject can breathe room air. The notches indicating inspiratory attempts do not show in all our tracings, though by observing our own reactions we feel sure that they occur. Their absence in some of the experiments may be explained by the fact that the rhythmic stimuli are not strong enough to cause the respiratory muscles to contract sufficiently to produce a change in the shape of the thoracic wall, so that a record would be made by the pneumograph. Apparently, the absence of the notches is not due to complete cessation of the respiratory stimuli.

In the distension experiments on ourselves we did not obtain any indication of the secondary or chemical apnoea, so well shown by Christiansen and Haldane. The failure of such an apnoea to occur in our subjects is, however, to be expected, as in neither of them is the most violent and prolonged forced breathing followed by apnoea.[10]

Figure VII is a tracing obtained from a normal dog. The tap is turned at various points in the respiratory cycle, so that the animal first breathed the air of the room, and then the air under pressure in the respiration apparatus. The upper curve is that written by the spirometer and the straight lines are made when the dog is breathing the room air. The lower curve is that ob-

[10] Boothby: Absence of apnoea after forced breathing. 1912, Jour. Physiol, xlv, 5, 328–337.

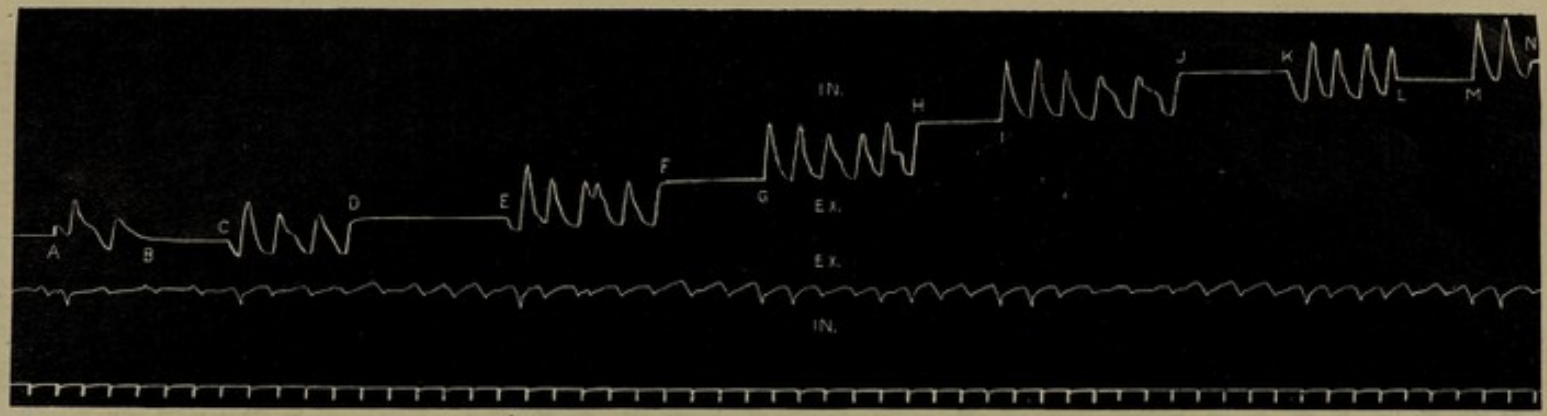

Fig. VII. Effect of distension on normal dog No. 1. Spirometer weighted to give 10 cm. water pressure. Upper curve written by the spirometer, with inspiration up. Lower curve written by the pneumograph, with inspiration down. At *A*, *C*, *E*, *G*, *I*, *K*, and *M* the tap was turned at various phases of the respiratory cycle, so that the dog breathed the air under pressure in the apparatus. At *B*, *D*, and etc., the tap was turned so that the dog breathed the room air, and the following horizontal lines do not indicate periods of apnoea, but that the animal is not at that time connected to the apparatus. No apnoea. Time in seconds.

Fig. VIII. Effect of distension on normal dog No. 1. Spirometer weighted to give 12 cm. water pressure. At *A* the tap turned so that the dog breathed the air under pressure. This was followed by an abortive expiration with a subsequent pause. At *B* the tap was turned to the room air. At *C* tap again turned to respiration apparatus. No apnoea. Time in seconds.

tained by means of the pneumograph. It does not show, as do those obtained from the human subjects, the change in the "Mittelage," because the length of the pneumograph necessitated its being passed over the chest of the dog and under the table on which the dog was lying. No evidence of inspiratory inhibition is seen here nor any sign of the primary distension apnoea shown by Christiansen and Haldane, and therefore resembles the curves obtained on ourselves.

Out of a long series of experiments on this same animal, only one presented a trace of expiratory difficulty, as shown in Figure VIII. It was the first experiment performed on this animal and two seconds elapsed before the dog was able to complete the expiration. After that the animal was ready to overcome the distension immediately, as did the human subjects mentioned above.

In the normal dog we were unable to obtain any example of the delayed or chemical apnoea following distension of the lungs.

In order to study the effect of increased intrapulmonary pressure with distension of the lungs, after division of the vagi, we used two dogs in which we had some three to four months previously divided the pulmonary branches of both vagi.

The results obtained from the dogs with the vagi divided in this manner were quite surprising. In one animal (No. 23), two out of seven experiments showed a primary apnoea on distension; one lasted six, and the other two and one-half seconds. Sixteen experiments were performed on the other dog, (No. 11); in nine of which there was no apnoea; in one an apnoea of one and one-half seconds; in three an apnoea of about three seconds, in one an apnoea of four and one-half seconds, and in two an apnoea of four and one-half seconds, occurring after several respirations.

In Figure IX is shown the longest primary apnoea obtained. The tap was turned so that the animal was suddenly made to breathe the compressed air. This was accompanied by dilatation of the thorax, as shown by the lower (pneumograph) curve, followed immediately by an incompleted expiration. The expiratory movement, however, does not expel any air as shown by the spirometer curve. The thorax remains stationary for

six seconds and the apnoeic period is finally broken by an inspiration. The next two respirations are somewhat slowed by a prolongation of the expiratory phase, after which the rhythm becomes quite normal.

Another example is given in Figure X, and a third in the first part of Figure XI in which the apnoeic period was broken by inspiration with distinct prolongation of the expiratory phase. It

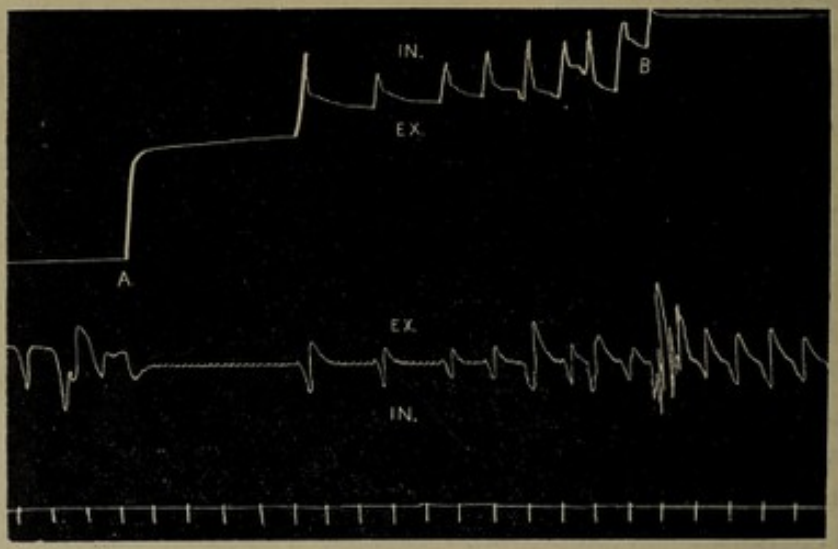

Fig. IX. Effect of distension on vagotomized dog No. 23. Spirometer weighted to give 12 cm. water pressure. Upper curve written by the spirometer, with inspiration up. Lower curve written by the pneumograph, with inspiration down. At *A* tap turned so that the animal breathed the air under pressure, causing an inspiration, followed by a partial expiration as shown by the pneumograph curve. After this there was a pause of six seconds broken by an inspiration. The pause was at the level of the following expirations. The subsequent respirations were slightly slowed and the expiratory phase was prolonged. Time in seconds.

is questionable whether the prolonged expiratory pause at *D* in Figure XI should be considered an example of the chemical apnoea of Christiansen and Haldane, or whether it is an exaggerated case of the prolonged expiratory phase seen in the first part of this figure and in Figures IX and X. On account of the relatively large dead space of the mask and connecting tubes, it seems unlikely that distension of the lungs would materially lower the alveolar carbon dioxide tension. We believe, therefore,

that this pause is similar to the other, though shorter, examples of a prolonged expiratory phase found in our vagotomized dogs and not an instance of a true chemical apnoea.

Our experiments on man supplement those of Christiansen and Haldane and together they show that a primary apnoea may or may not occur in normal individuals upon distension of the lungs.

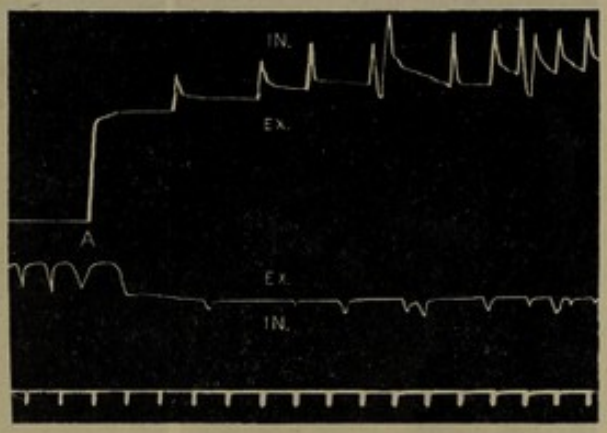

Fig. X. Effect of distension on vagotomized dog No. 23. Spirometer weighted to give 12 cm. water pressure. Upper curve written by spirometer, with inspiration up. Lower curve written by pneumograph, with inspiration down. The upper pointer is writing to the left of the lower pointer. At *A* the tap turned so that the animal breathed the air under pressure, causing an inspiration, followed by a pause of two and one-half seconds, broken by an inspiration. The next respiration shows a prolonged expiratory phase, as do the following to a lesser degree. Time in seconds.

Our experiments on two dogs in which the pulmonary branches of both vagi were divided and in which we obtained several instances of a short apnoea on distension of the lungs is direct evidence against the theory that the vagi transmit impulses which arise from distension of the lungs and thereby inhibit inspiration. Our curves on the vagotomized dogs are all the more suggestive because the apnoea, when it does occur, is at the end of the following partial or complete expiration which is broken by an inspiration. They suggest quite strongly that there is a condition of inspiratory inhibition. If so, it can not be due to impulses arising in the lungs and passing over the vagi, as the pulmonary branches are all divided.

In another paper from this laboratory by Boothby and Shamoff,[11]

[11] Boothby and Shamoff: A study of the late effect of division of the pulmonary branches of the vagus nerve on the gaseous metabolism, gas exchange, and respiratory mechanism in dogs. This Journal, 1915, xxxvii.

other experiments are reported which show that the pulmonary branches of the vagus nerve do not transmit impulses that control functions in any way essential to life. And more specifically the nerve does not possess any demonstrable power over the normal regulation of the gaseous metabolism, the pulmonary ventilation, or the gas exchange in the lungs.

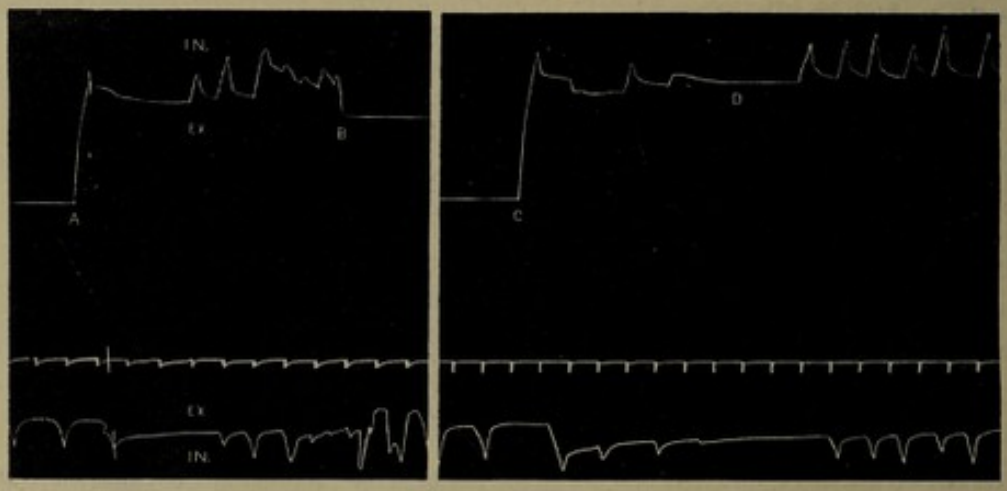

Fig. XI. Effect of distension on vagotomized dog No. 11. Spirometer weighted to give 12 cm. water pressure. The upper curve written by the spirometer, with inspiration up. Lower curve written by the pneumograph, with inspiration down. Upper pointer is writing to the left of the lower pointer. At *A* and *C* tap turned so that the animal breathed the air under pressure. At *A* the first effect of distension is expansion of the chest, followed by a slight contraction after which there is a pause of about three seconds broken by an inspiration. The pause is on a level with the bottom of the following expirations. At *C* the inspiration following the distension is more marked and is again repeated in about a second followed by a pause of about two seconds. This is broken by an inspiration followed by a prolongation of the expiratory phase. The next expiratory phase is very much prolonged (4 secs.). The respirations then become quite normal. Time in seconds.

The experiments reported in this paper indicate that the nerve does not transmit impulses which, according to the theory of Hering and Breuer, arise from distension of the lungs and inhibit inspiration.

Respiration is the result of a highly coordinated response of many muscles to the need of the body for a constant exchange of gases to and from the air. It is normally an involuntary and

rhythmic act under the control of what has been designated as the respiratory centre and what we prefer to call the ventilation centre. Respiratory rhythm, unlike cardiac rhythm, must be easily and instantaneously modified to meet the needs of an entirely different order, such as phonation, delugition, and the application of external force to the thorax. Therefore the rhythmic stimuli sent out by the ventilation centre must be weak, so that stimuli from any other source may instantly halt or change the respiratory movement at any stage of the cycle.

In different individuals the strength of the rhythmic stimuli sent out by the centre may readily vary. Certain other stimuli may affect the respiratory rhythm in one person with greater rapidity and in quite a different way from that in another person.

Inspiration under usual conditions is a muscular act and consists in distending the thorax with a disturbance of elastic equilibrium. Expiration, on the other hand, when the body is at complete rest, is largely a passive act and is the return of the thorax to its former position of elastic equilibrium.

Under many circumstances, however, such as work, phonation, breathing against an obstructed air-way or against positive pressure, expiration is no longer passive but active and must, therefore, be performed by the contraction of the expiratory group of muscles. Inspiration may then become the passive act.

In the human subjects and in the normal dog studied by us, the expiratory group of muscles were almost always in tone and ready for work, and the rhythmic expiratory stimulus was of sufficient strength to cause them to contract normally in spite of an additional and instantaneous overload. On the other hand, with the subjects studied by Christiansen and Haldane, some thirty seconds elapsed before the centre sent out stimuli sufficiently strong to cause the expiratory muscles to contract against the sudden overload. That is, in those subjects the time reaction was slow. In other words, it took thirty seconds for the ventilation centre to become adjusted, probably through the coordinating action of some higher centre, so that stimuli of sufficient strength would be sent out to cause muscular contraction of the expiratory muscles.

In the dogs with divided vagi the expiratory muscles started to contract the moment the inspiration was completed. This contraction is seen distinctly in the pneumograph curve in Figure IX but is only slightly indicated in Figure X. The expiratory impulses sent out by the centre were strong enough to keep the thorax contracted to a certain level but could not carry it further. In this instance the failure to expire completely does not seem to be due to lack of proper stimuli but to actual inability of the muscles to contract more against the increased resistance, because the later expirations do not reach a lower level. In these experiments the respiratory centre was sending out stimuli that kept the expiratory muscles contracted to a certain level. The stimuli or the muscles themselves were, however, unable to complete the expiratory act. It is very probable that the apnoea lasted until the automatic ventilation centre received impulses from some higher coordinating centre so that the action of the ventilation centre was reversed and stimuli sent out to the inspiratory group of muscles.

In the experiments performed by us on the dogs without any pulmonary vagal supply, these nerves had been divided several months previously, so that the animals had had time to readjust themselves to the loss of vagal activity. It is well known, as has been shown by Gad[12] and others, that immediately following freezing or dividing the vagi there is a distinct change in the respiratory rhythm and the form of the respiratory curve. After division of one vagus, the return to normal takes place usually within one or two minutes. Lewandowsky[13] shows tracings taken five and again twenty-four hours after division of both vagi in the neck; in the first, there is still a distinct variation from the normal, but in the second, the character of the respiratory curve has returned to normal, though it is still a trifle deeper and slightly slower.

[12] Gad: Die Regulirung der normalen Athmung. Arch. f. Physiol., 1880, 1–30.

[13] Lewandowsky: Die Regulirung der Athmung. Arch. f. Physiol., 1896, 4, 196–248; 483–510. Tracings 64, 65, 66.

The vagus nerve undoubtedly has some important function in respiration and the interruption of that function produces temporary changes in the respiratory rhythm. This may readily be conceived to occur even if its normal function is in no way concerned with transmitting impulses that arise from dilatation or collapse of the lungs. It may well be, as maintained by Krogh,[14] that the nerve has in the lungs a vasomotor function; or, as suggested by Brodie and Dixon,[15] it may be concerned with the dilatation and constriction of the bronchioles; or it is not unlikely that it might be concerned with both these functions.

The cause of the primitive rhythmic activity of the ventilation centre is unknown. It is recognized, however, that the rhythm and the volume of the respiration are influenced by many factors, the chief of which is the hydrogen ion concentration of the blood passing through the ventilation centre. The secondary factors influencing the centre are stimuli which enter the central nervous system over nearly every centripetal nerve[16] in the body and which are probably modified by a most complex and practically unknown coordinating mechanism.

SUMMARY

In this paper we have studied the effect of distension of the lungs on the respiratory rhythm in man and in normal and vagotomized dogs. We were unable to obtain any evidence to substantiate the theory suggested by Hering and Breuer that distension inhibited inspiration by the stimulation of the intrapulmonary endings of the vagus nerve.

[14] Krogh: On the mechanism of the gas exchange in the lungs of the tortoise. Skand. Arch. f. Physiol., 1909, xxiii, 200–216.

[15] Brodie and Dixon: The bronchial muscles, their innervation, and the action of drugs upon them. Jour. Physiol., 1903, xxix, 97–173.

[16] Sjöblorn, J. Ch.: Exp. Untersuchungen uber den Einfluss einiger Zentripetale Nerven auf die Athmung. Skand. Arch. f. Physiol., 1914, xxxii, 1–114.

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