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MECHANISM

OF

Reflex Nervous Action

IN NORMAL RESPIRATION.

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MECHANISM OF REFLEX NERVOUS ACTION IN NORMAL RESPIRATION.

An Address Delivered February 16, 1874, before the New York Society of Neurology and Electrology, by Austin Flint, Jr., M.D., Professor of Physiology in the Bellevue Hospital Medical College, New York.

Phonographically Reported by Geo. W. Wells, M.D., of New York.

MR. PRESIDENT, and Gentlemen of the Society: I shall have the honor, this evening, of making some remarks on the mechanism of nervous reflex action in normal respiration. A great part of the statements that I shall make, and the views advanced upon this subject, are derived from personal experimentation; but they are by no means entirely new, for many of the experiments upon which my views are based were published in the *American Journal of Medical Sciences*, in October, 1861. Still, these experiments, which seem to me to be of considerable importance, have been noticed so little in physiological writings, that I venture to assume that they may be new to many of those who now listen to me.

After Marshall Hall had formularized the ideas of certain of his predecessors, with regard to what he termed reflex action, it was pretty generally understood by physiologists that the movements of respiration were of a purely reflex character, unless they were modified by voluntary acts; and that the ordinary movements of respiration, which take place without the intervention of the will, were entirely reflex.

The experiments that I shall detail this evening were based upon, or, rather, suggested by, an experiment made in 1664, by the celebrated Robert Hooke, and published in the *Philosophical Transactions*, for 1667. This experiment, though it could not be completely understood at the time it was made,

in 1664, is very instructive. It consisted in introducing a bellows into the trachea of a dog, making an opening into the chest, cutting off a portion of the lungs, and forcing air through them; and it was found that, so long as air was forced through the lungs in this way, the animal, though sensible, made no efforts at respiration. I may here anticipate enough to say that I shall assume that, in this experiment, while air was supplied to the system, the animal felt no want of it, had no inclination to respire, and consequently did not respire.

In studying the subject of the reflex nervous action in respiration, we are immediately struck with the anatomical relations of the pneumogastric nerves to the respiratory apparatus; and it is all the more important to study the relations of these nerves to the process of respiration, as they arise near that point in the medulla oblongata where the so-called "vital knot," or the respiratory nervous centre, is supposed to be situated.

It might be opportune, perhaps, to rapidly sketch the condition of our knowledge respecting the influence of the pneumogastric nerve upon respiration.

As you all know, the pneumogastric nerve is one of immensely wide distribution, and is connected with various distinct functions. The branches that are distributed to the respiratory organs are the following:

The superior laryngeals, which are distributed to the mucous membrane of the larynx and the membrane covering the top of the larynx, sending off a branch on either side to the crico-thyroid muscle, this branch being a mixed nerve.

Next in order, we have the inferior, or recurrent laryngeal nerves, which are distributed to all the intrinsic muscles of the larynx, except the crico-thyroid. These nerves are composed entirely of motor filaments, and are derived from a variety of sources. The experiments of Bernard, which have been so often repeated by Dr. Dalton, myself, and others, of extirpating the spinal accessory nerves, or the section of the communicating branches to the pneumogastrics, show that this is the nerve of phonation; and the filaments that preside over the voice pass to the larynx through the recurrent laryngeals.

Then we have, distributed to the lungs themselves, the anterior and posterior pulmonary branches, which go, almost ex-

clusively, to the mucous membrane of the pulmonary structure. These branches communicate with the sympathetic; but, according to Sappey, they do not go to the walls of the blood-vessels, being distributed to the mucous membrane lining the air-vesicles.

So much for the distribution, in general terms, of those branches of the pneumogastrics which go to the lungs; and this distribution being so extensive, you can readily see that we can hardly discuss the reflex nervous action in respiration, without taking the action of these nerves into consideration.

The pneumogastric is originally an exclusively sensory nerve. Experiments are somewhat obscure upon this point, on account of the difficulty in irritating the original roots of the pneumogastrics, without involving filaments of other nerves; still, the careful experiments of Longet showed that when the spinal cord of animals is opened, and the roots of the pneumogastrics are carefully isolated and stimulated, no movements follow their irritation. This shows that the original filaments of the pneumogastric are not motor. But the pneumogastric, as it emerges from the cranial cavity, receives numerous communicating motor filaments, and thus, in its course, it is a mixed nerve. Following out the filaments that are distributed to the respiratory apparatus, we find that the filaments from the superior laryngeal going to the crico-thyroid muscle, are almost exclusively motor; the motor filaments of the recurrents go to the intrinsic muscles of the larynx, whereas the true pulmonary branches are distributed to the mucous membrane. Therefore, excluding the movements of the larynx, the action of the pneumogastric in the reflex phenomena of respiration, theoretically, would be that of a sensory nerve, conveying to the respiratory nervous centre an impression, or sensation, which gives rise to the movements of respiration.

If both pneumogastrics, however, be divided, we find that the respiratory movements are very much diminished in frequency; and I have in my mind an experiment in which they were reduced from twenty-four to four or six in a minute; yet, they still continue; and this simple experiment, so often performed as a class-demonstration, is a denial of the proposition that the pneumogastric nerves are the only nerves for

the transmission of the so-called *besoin de respirer*, or sense of want of air, to the respiratory nervous centre. If the pneumogastrics were the only nerves which have this function, respiration should cease after their division; but it does not.

I do not think that physiologists are at present able to explain the cause of the great diminution in frequency of the respiratory movements, after the division of both pneumogastric nerves; but this is, nevertheless, an invariable phenomenon. In the experiment to which I have referred, curiously enough, the animal did not die; and when I presented him to the class, some three weeks after the section of the nerves, the number of respirations had returned to the normal standard. I imagine that a reunion of the two ends of the divided nerve had occurred. A post-mortem examination (the animal being sacrificed in another experiment) showed that the nerves, though not, perhaps, completely united, had formed a partial union, at least, between the divided extremities.

The condition of the lungs after the division of the pneumogastrics, that is, in cases where death follows such division, is peculiar, and was, for a long time, unexplained by physiologists. In animals that live for three or four days and subsequently die, the lungs present pretty generally, throughout their entire substance, a carnified condition. They are solid; will sink in water; but still do not present evidences of inflammation. It was thought, at first, that this was due to inflammation; but physiologists failed to find the positive evidence of any such action. Bernard, I think, has given the correct explanation of this peculiar appearance. He observed that, when the respiratory movements are gradually diminished in frequency, they are immensely increased in intensity; that the inspirations are remarkably prolonged and profound; and that the chest, in the inspiratory act, is extraordinarily distended. He advanced the idea that this extreme dilatation of the air-cells induced capillary hæmorrhage in certain parts of the lungs; that, as this extended, the blood coagulated; and, finally, the lungs became almost solid.

Galvanization of both pneumogastrics in the neck arrests the respiratory movements, if it be powerful; and this action is reflex, not direct. If the nerves be divided, galvanism of

their peripheral extremities has no effect on respiration, though it arrests the action of the heart; whereas galvanization of the central ends arrests respiration in the same way as galvanization of the nerves before their division. Galvanization of the superior laryngeal nerves arrests respiration, and renders the animal motionless. This effect follows powerful galvanization of any of the sensitive nerves, though not so certainly and promptly as galvanization of the superior laryngeals. If the superior laryngeals be powerfully galvanized, respiration stops immediately, and is arrested at the instant the current is applied, but more easily during inspiration than expiration. This arrest of the respiratory movements is particularly marked as regards the action of the diaphragm. I have made these preliminary remarks to show that there is very little known with regard to the reflex phenomena of respiration, operating through the pneumogastrics.

Although the proposition that I am about to enunciate has been denied by a few physiologists, still, the greater number believe that the medulla oblongata is the respiratory nervous centre. Adopting this view, which is almost universally accepted, the mechanism of the reflex phenomena of respiration may be briefly stated as follows:

These phenomena require three conditions:

1. The physiological integrity of nervous filaments conveying an impression, or sense, to the nervous centre.

2. The existence and physiological integrity of the nervous centre.

3. Finally, the physiological integrity of the motor nerves which convey the stimulus that is generated at this nervous centre to the respiratory muscles.

If we assume that respiration involves a reflex action, we must admit that there are nerves which convey certain impressions to the medulla oblongata. We find that the medulla oblongata is the respiratory centre; for, when this centre is destroyed, the movements of inspiration instantly and permanently cease. A single series of experiments has been published by Dr. Brown-Sequard, which are assumed to prove that respiratory movements may occasionally persist after destruction of the medulla oblongata; they have never been

confirmed, and cannot be accepted as demonstrating that the medulla oblongata is not the centre for respiration.

The sensation which we experience of want of air has been called, by the French, the *besoin de respirer*. It might be well enough to call it the sense of the want of air; but, under ordinary circumstances, when respiration is free, when the surrounding air is pure and in abundance, this sensation is not felt, except at the medulla oblongata. This impression, however, at proper intervals, is conveyed to the medulla, and keeps up the respiratory movements, without our knowledge; and it is only when there is a greater deficiency of air than usual, or when there is an obstruction to respiration, that we feel this sense of want of air as a positive sensation, in the form of a sense of suffocation, more or less pronounced. I think that the old experiment of Robert Hooke established this point; and it certainly demonstrates it, when taken in connection with what we have learned of late years.

In Robert Hooke's experiment, the dog was supplied artificially with air, completely and efficiently; and he noticed that, so long as he supplied the respiratory needs, though the animal looked around and was entirely sensible, he made no respiratory efforts. This showed that, during the free passage of air through the lungs, the want of air was not felt by the medulla oblongata, and there was no stimulus to produce respiratory movements. There was no necessity felt for respiratory movements, and none took place. This experiment suggested my own observations, in 1860–61. I put an animal, a dog, completely under the influence of ether; introduced the nozzle of a bellows into the trachea; opened the chest; turned back the anterior walls, by breaking the ribs, so that I exposed the lungs and diaphragm, and then very carefully maintained artificial respiration. I found that while artificial respiration was complete and efficient, the animal remained perfectly quiet, and made no respiratory efforts. I could see, in this experiment, the slightest movement of the diaphragm. I then interrupted the artificial respiration for a moment. Very soon I could see the diaphragm begin to quiver; it contracted, at first, slightly; then more and more powerfully and rhythmically; and the animal finally opened the mouth and made ineffectual efforts

to breathe. I then resumed the artificial respiration, and in a short time the animal became quiet, when the respiratory needs were entirely supplied.

I then exposed an artery, and introduced in it a stop-cock, so that I could take blood from the vessel at will. While I kept up artificial respiration, I drew a little blood from the artery upon a white plate. It had all the characters of pure arterial blood. I then had my assistant, who was working the bellows, stop the artificial respiration, and I allowed the blood to flow in a small stream from the artery. I found, always and invariably, that when the blood began to be dark in the artery, and not before, the animal made efforts to respire.

There are several views, which have been advanced by physiologists from time to time, as to the location of the *besoin de respirer*.

Marshall Hall and some others thought that it was due to a want of air in the lungs themselves, and that this want was conveyed by the pneumogastric nerves to the medulla oblongata; but I do not see how, with this supposition, it is possible to explain respiratory movements which occur after division of both pneumogastrics.

Reid thought that the sense of want of air was due to the circulation of venous blood in the medulla oblongata; a view which is entirely theoretical and incapable of positive demonstration.

Berard thought that the sense of want of air, or the *besoin de respirer*, was due to the distension of the left side of the heart by venous blood when respiration was arrested. In support of this view, he brought forward the well-known fact that, in certain cases of disease of the heart, even when the lungs are perfectly normal and completely filled with air, there is frequently a sense of suffocation.

Vierordt thought that the sense of want of air was due to the circulation of venous blood in the substance of the nerves themselves.

Volkmann, in 1842, made the very important observation, that an animal experiences the sense of suffocation, when deprived of air, after division of both pneumogastrics. This fact was well known. Every one who has divided both pneumogastric

nerves in a cat must have noted that the animal experiences intense distress from suffocation. In this animal, the cartilages of the larynx are very flexible, and paralysis of both recurrent laryngeal nerves, which follows division of the pneumogastrics in the neck, causes the glottis to close in inspiration, so that the animal is almost immediately deprived of air. Volkmann reasoned, from this fact, which had often been observed before, that the sense of want of air resides in the general system, and is not to be referred to any particular organ or organs.

If I may be permitted, now, to continue the account of my own experiment, I think I can show that it is certain that the sense of want of air resides in the general system; and, furthermore, that it is due to a want of oxygen in the general system.

Here we have an animal with the heart and lungs exposed; a bellows placed in the trachea, and artificial respiration maintained; but there are no efforts at breathing, so long as air is supplied in sufficient quantity. We put a stop-cock in the artery, and, while artificial respiration is continued, there is the natural red color to the blood. But we stop the respiration, and we find that, just so soon, and no sooner, as the blood becomes markedly dark in the arteries, the animal begins to make efforts at respiration, and feels the sense of want of air. I think this experiment shows that the sense of want of air is due to the circulation in the system of blood more or less venous in its character. I say I think it shows this fact; I am sure it shows it, in connection with the other facts bearing upon the question.

What is the cause of this sense of want of air, and what are the conditions of the blood that are different from the conditions during efficient artificial respiration? Of course, whatever they may be, these two conditions are present: one, a deficiency of oxygen in the blood, that is rendered more or less venous; and another, the presence in the arteries of blood containing an excess of carbonic acid. The question now arises, whether the sense of want of air be due to a deficiency of oxygen in the system, or to the irritating qualities of carbonic acid. How can we separate these two conditions, experimentally, and how can we deprive the tissues of oxygen, without supplying blood charged with carbonic acid? A very

simple way is to drain the system of blood; for, if blood get to the system, there is no question but that oxygen will be carried to the tissues, it being always conveyed by the blood, and by the blood alone. Therefore, if the system be deprived of blood, no oxygen can get to the tissues. Again, if we drain the system of blood by cutting out the heart, we answer the question whether or not the sense of want of air be due to the distension of the left side of the heart by venous blood. If you take this same animal, that is not breathing, and in which the respiration is kept up by the bellows, and tie a ligature around the aorta, he begins to breathe, although the lungs are supplied with air, for the reason that the oxygen-carrying blood is cut off from the system. If, now, in this same animal, we suddenly cut out the heart, the system is, of course, almost instantly drained of blood, and the animal always makes violent and repeated respiratory efforts, although the lungs are fully supplied with air. It seems to me that these experiments show conclusively that the sense of want of air is derived from the general system; that it is due to a want of oxygen in the system, and not to the irritating properties of carbonic acid; and that this sense is entirely analogous to the sense of hunger and the sense of thirst. The sensations of hunger and of thirst are subjectively referred to the stomach or to the mouth and fauces; but they really reside in the general system. If a fistula be made in the stomach of a dog, and if the animal be allowed to drink, after having been deprived of water for a day or two, the water will flow out through the fistula as fast as it is taken into the stomach; and, although the animal will continue to drink, the water is not absorbed, and the thirst is not satisfied. I have seen animals drink, in this way, gallons of water, being satisfied with a moderate quantity after the fistula has been closed. Also, if food be taken into the stomach and not absorbed, the sense of hunger is only momentarily appeased; but this sense is referred to the stomach, because food is naturally introduced into the system by the stomach. So the sense of want of air, which I believe to be due to the want of oxygen in the tissues, is referred to the respiratory organs, because it is by filling the thorax that we naturally supply this deficiency in the system. If the sense of want of air be exaggerated,

it constitutes the sense of suffocation; and this is one of the most distressing sensations of which we have any knowledge.

It has been observed that convulsions very often follow hæmorrhage; and this fact has been found very difficult of explanation. But hæmorrhage is really suffocation; and convulsions are generally observed in suffocation. It makes very little difference, practically, whether we drain the system of the oxygen-carrying fluid, or whether we prevent oxygen from going to the lungs; we have, in each case, the same result, as far as respiration is concerned; and, in death from profuse or sudden hæmorrhage, it seems to me that the convulsions are, in fact, no more than convulsions due to suffocation. This view seems to offer a satisfactory explanation of the convulsions following hæmorrhage. There is one point, however, in this connection, which is interesting, and which I appreciate as fully as any one who now hears me.

I have assumed that draining the system of blood, by preventing the oxygen from getting to the system without carrying to the tissues carbonic acid, proves that the sense of the want of air is due to a want of oxygen in the tissues, and not to the stimulation of carbonic acid. Carbonic acid does not originate in the blood, and is undoubtedly an excretion. If we take a muscle cut from a living frog, and put it under a bell-glass containing oxygen, even though it contain no blood, this muscle will respire. Again, if we put the same muscle in an atmosphere of hydrogen, we find that a certain amount of carbonic acid is given off. In normal nutrition, carbonic acid is carried away from the tissues, almost as soon as it is formed, by the blood. If, then, the system be drained of blood, what is to prevent the carbonic acid from accumulating in the tissues, and may not this be the cause of the sense of want of air?

I have tried to imagine experiments to meet this objection. I have tried to devise some means of getting rid of the carbonic acid from the tissues, that will not, at the same time, either supply the oxygen, or send through the tissues a fluid like blood, containing carbonic acid. This flaw in my argument I cannot correct experimentally.

One other important point in this connection, which may

be of more interest to some of my hearers than those to which I have thus far called your attention, is the cause of the first respiratory effort made by the new-born child.

Many of the ancient writers regarded the placenta as the respiratory organ of the fœtus; and we now know positively, that the fœtus *in utero* gets its oxygen from the blood of the mother through the placental vessels; but when the child is born, this source of supply of oxygen is cut off, and the first act of pulmonary respiration is performed, this being the commencement of the function which continues to the end of life.

What is the exciting cause of this first respiration? It has been shown positively, by experiments upon animals, that the first respiration is due to an arrest of the placental circulation. I have frequently opened the abdomen of dogs and cats, big with young, and taken the young from the uterus, when they had hardly attained one-fourth of their size at term; have laid them on the table, and respiratory movements have always occurred in a very short time after they were separated from the mother. Experiments have been made upon animals, by opening the abdomen and pressing upon the umbilical cord, and in a short time, respiratory movements have occurred.

It is well known to gynæcologists and obstetricians that respiratory movements occasionally occur in the human fœtus, *in utero*, as a consequence of some interference with the placental circulation; and the amniotic fluid, and even meconium, have been found in the respiratory passages.

A very thorough exposition of these facts has lately been made by Dr. B. S. Shultze, in a work published at Jena, in 1871, entitled *Der Scheintod Neugeborener*, in which the points I have stated are so fully set forth that there can be no doubt upon the subject. It seems to me that the respiratory efforts before birth constitute a very strong argument in favor of the view that I have stated; and it seems to me certain that the first respiratory movements after birth are due to the following conditions: The placental circulation is arrested; the new being feels the sense of the want of air; and the impression is conveyed to the medulla oblongata, where a stimulus is generated which is carried by motor nerves to the

respiratory muscles. The respiratory muscles then contract, and thus the lungs are, for the first time, distended with air.

The general results of the experiments that I have detailed this evening, and which, I may say, I have performed over and over again, are the following:

Respiration is a reflex phenomenon. The movements of respiration are reflex. There is a special respiratory nerve centre, which is situated in the medulla oblongata. When this nervous centre is destroyed, no respiratory movements can take place, because there is no centre to receive the impression of want of air. Respiratory movements are due to an impression made upon the centripetal nerves; and this impression is due to a want of oxygen in the general system. The sympathetic system may possibly be involved in this action, but this point has not been determined. The sense of the want of air, conveyed to the medulla oblongata, gives rise, under ordinary conditions, to respiratory movements, which take place without the consciousness of the individual. Under ordinary conditions, respiration is carried on by the medulla oblongata, and does not involve the action of the brain. Whenever there is any difficulty in respiration, the sense of want of air is exaggerated, until it constitutes a sense of suffocation, which involves voluntary efforts on the part of the individual to supply this want of air.