

ESSAY.

by

James Norman Davidson,



THE HISTORY OF OUR KNOWLEDGE OF THE NERVOUS AND
MUSCULAR MECHANISMS OF RESPIRATION.

An Essay submitted for the Wellcome Prize for
the History of Medicine (1932).

by

J. NORMAN DAVIDSON.

Member of the History of Medicine Class
Autumn Term 1931.



1. VENTILATION.

In considering this subject we are faced at the outset with a difficulty inasmuch as we must restrict ourselves in this essay to the nervous and muscular mechanics of respiration and must neglect the chemical aspect with which the other two are intimately correlated.

"In breathing there are two kinds of blessings: inhaling the air and exhaling it; the former is oppressive, the latter refreshing; so strangely is life mingled."

GOETHE.

I. PRELIMINARY.

In considering this subject we are faced at the outset with a difficulty inasmuch as we must restrict ourselves in this essay to the nervous and muscular mechanisms of respiration and must neglect the chemical aspect with which the other two are intimately correlated. So intimate indeed is the interrelationship between the various mechanisms in the normal functioning of the body that we offer no excuse for digressing here and there to deal with topics which may appear extraneous but which nevertheless have a certain amount of bearing on our main theme. The fact so often emphasised by Sir J. Arthur Thomson that we must not confine the sciences to watertight compartments is especially true of Physiology where the relationship to the allied sciences of Chemistry, Physics, and Anatomy, is of such a degree of intimacy that the proper appreciation of a physiological topic requires a moderate, if not extensive, understanding of the relationships which the other sciences bear to it. Particularly is this true of Respiration where, in order to appreciate the nervous and

muscular mechanisms, we must have some acquaintance with the respiratory gases, with the atmosphere which we breathe, with the anatomy of the respiratory system and with those chemical changes which take place, both in the lungs where the inspired air comes into such close contact with the circulating blood and in the tissues bathed by that blood.

It is a curious fact that although something was known of the mechanism of respiration at a very early date, the uses of respiration were not fully established till a much later period. The early ideas of the purposes of breathing were many and varied. Some said that its purpose was to cool the heart; others, that the movement of the lungs acted as a pump, driving blood from the right to the left side of the heart; others, that the motion of the lungs kept the blood mixed and prevented the separation of serum from the more solid constituents of the blood; but it was not until the time of Mayow that the true function of respiration, the aeration of the blood, and the removal from it of carbon dioxide was established.

The first of the above views on the function of respiration was that held by Galen. He considered that air was drawn into the lungs and thence passed into the pulmonary artery which led it to the left side of the heart where it mixed with the blood, filling it ^{with} 'vital spirits' derived from the fire which burned continuously in the heart during life. This fire was cooled and regulated by the stream of air from the lungs. These views were held even as late as the time of Vesalius who, however, showed signs of doubting their validity. ^{1) *}

Fabricius ²⁾ was a staunch upholder of the views of Galen but these views were completely overthrown by Harvey in his famous work on the circulation of the blood. ³⁾ Servetus ⁴⁾ before him, and also Matthew Realdus Columbus ⁵⁾ had however understood the pulmonary circulation and had proved that blood passed from right to left sides of the heart through the lungs and not through the interauricular septum.

interauricular

* These numbers refer to the Bibliography at the end.

veins

Vesalius ¹⁾ noticed the obliquity of the ribs and Fabricius ²⁾ saw that this led to an increase in the distance between adjacent ribs when these were pulled up. This action, he considered, was brought about by equal activity of external and internal intercostal muscles. He also considered that in normal respiration the diaphragm alone acted, the intercostals coming in to play only in forced respiration and cited as proof cases in which he had found the ribs ossified to the sternum and to the vertebrae and so incapable of movement.

It was not however till the beginning of the seventeenth century that the mechanism of respiration received the detailed attention of physiologists.

³⁾ was one of the earliest to realize the true function of the respiratory movements. His book "De usu animalium" treated the mechanics of muscular activity for the first time in a really thorough manner, although the subject had been studied previously by various men including Fabricius, Vesalius and Steensen. ⁴⁾ These mechanics applied to the

II. THE SEVENTEENTH CENTURY.

Possibly the most important physiological event of the 17th century was the discovery by Harvey of the circulation of the blood, but although he realised that the blood passed from right to left sides of the heart through the lungs and at the same time changed from the venous to the arterial condition yet he did not realise the part played by the movements of the lungs.³⁾

Van Helmont (1557-1644) thought that in the lungs the blood suffered a fermentation whereby its colour became lighter, a fermentation preparatory to that by which the vital spirits were introduced in the left side of the heart,⁶⁾ but Borelli (1608-79) was one of the earliest to realise the true function of the respiratory movements.⁷⁾ His book "De motu animalium" treated the mechanics of muscular activity for the first time in a really thorough manner, although the subject had been studied previously²⁾ by various men including Fabricius⁸⁾ , Vesalius⁸⁾ and Stensen⁹⁾ . These mechanics applied to the

muscles of the chest at once dispelled all notions that the purpose of the lungs was the cooling of the heart or the expulsion of noxious vapours generated by the innate fire of the heart, and showed that the contraction of the muscles of the chest resulted in an increase in the capacity of the thorax and a consequent influx of air under the influence of atmosphere pressure. Borelli noticed the peculiar articulation of the ribs, and that the sternum was not fixed but could move up with them. He considered that in normal inspiration the diaphragm and the intercostal muscles cooperated and that these two factors were alone responsible not only for normal, but for forced inspiration. Normal inspiration then was caused by the diaphragm and intercostal muscles acting together, both sets of intercostals on contraction raising the ribs. Here he was in conflict with other men of his time notably Willis and Swammerdam¹⁰⁾ who held that the two sets of intercostal muscles had opposite actions, the external raising the ribs and the internal lowering them. The question arose later as we shall see.

Borelli, then, assumed that both sets of intercostals varied the ribs causing the sternum to rise so that the diameter of the thorax was increased anteroposteriorly, while it was increased from side to side by the turning out of the ribs owing to their peculiar articulation. The diaphragm also contracted, its arch becoming flattened while its central tendon remained stationary, pulling the ribs down slightly and increasing the depth of the thorax. All these actions resulted in an increase in the volume of the thorax, and diminutive of air pressure within so that the lungs were expanded by the air forced into them through the trachea by atmospheric pressure.

long /

Robert Boyle about 1660 performed some fundamental experiments on respiration by means of the air pump ¹¹⁾. By placing animals in a vessel in which a vacuum could be created he showed that life ceased on removal of air, and by comparing the effects on animals with that on a lighted candle he showed that similar changes took place in both cases and that the process of respiration resembled a combustion. His experiments on animals in vacuo were later followed

up by Hales ¹²⁾. One of his assistants, Hooke, (1635-1702), an early experimenter with the microscope, performed some epoch making experiments on respiration. ¹³⁾

He cut away a considerable portion of ribs and diaphragm of a dog and inserted the nozzle of a bellows in the trachea and by pumping air in and out of the lungs he found that life could be maintained for a considerable time, but that when blowing ceased convulsions occurred and the animal showed signs of collapse. He had therefore proved that it was the movements of the lungs which were necessary for life and not those of the chest, the latter merely serving to bring about the former. He then altered his bellows so that a continuous blast of air passed into the lungs which were pierced to allow of its escape. Life was maintained in a normal manner but convulsions occurred when the blast was stopped. After cutting out a piece of the lungs he noticed that the blood circulated through the lungs both when they were extended and when they were collapsed. He came to the conclusion that

the motion of the lungs was not necessary for life. When death followed the stoppage of the blast it was caused not by the cessation of lung movements, nor by the stopping of the circulation through the lungs, but by lack of a supply of fresh air.

About the same time Richard Lower published his "Tractatus de Corde" which was probably the greatest advance in the study of the circulation since the time of Harvey. He showed by experiments similar to those of Hooke that blood changed from dark red to bright red on passing through the lungs and not in the heart as was previously thought ¹⁴⁾. He came to the conclusion along with Borelli that blood passing through the lungs took up air and that consequently fresh air, must be continuously supplied to the living organism for the maintenance of life. Lower ¹⁵⁾ also investigated the mechanism of respiration. He cut the phrenic nerve in the dog and noticed that the animal's subsequent behaviour corresponded to that of a broken winded horse. Diaphragmatic respiration ceased and the main

burden of respiratory work was thrown on the intercostal muscles so that during exertion breathing was rendered very difficult and was accompanied by great straining of the chest wall.

These experiments were being carried on at the same time as Malpighi was making important discoveries in the nature of the lung tissue ¹⁶⁾. One of the first men to realise that only a part of the air was utilised in respiration was John Mayow. Born in 1643 and educated at Oxford, he practised as a Lawyer but spent a great deal of time engaging in physiological research. In 1668 he published his *Tractatus Quinque* of which the second one, 'De respiratione' is of most interest to us here. In the first tract "de sal nitro et spiritu nitro aëro" he showed that nitre could be made to yield a 'nitro aerial spirit' (oxygen) which was a constituent of atmospheric air and which was used up in the breathing of animals and also in the combustion of a candle. He concluded that a portion of the air ("the nitro-aerial particles") was necessary for life and for combustion and that



Portrait of Mayow.

when it was used up life and combustion ceased. They also ceased if the particles were removed by evacuation of the vessel by pumping as was done by Boyle. Thus the similarity between respiration and combustion was becoming more and more manifest. ¹⁷⁾ A knowledge of respiration had been shown in the works of several men of the period; Highmore ¹⁸⁾, Spigelius ¹⁹⁾ and especially Sylvius ²⁰⁾ but Mayow's views on respiration were a much more definite continuation of those of Sylvius. He followed up Boyle's experiments on atmospheric pressure and fully understood the reason for the passage of air into the lungs on inspiration viz. the capacity of the thorax was increased by the action of the muscles of the chest wall so that the atmospheric pressure forced air down the trachea and into the lungs distending them and neutralising the tendency for a vacuum to be produced within the chest. To demonstrate this he used an apparatus similar to that in ^{use} ~~one~~ today under the name of Donder's model. ²¹⁾ He explained the muscular action of inspiration thus:- at the end of expiration the

ribs pass obliquely down from the spine to the sternum. When the intercostal muscles contract the ribs are pulled upwards, and the distance between adjacent ribs is thereby increased, the sternum is raised, and the ribs, by virtue of their peculiar articulation to the vertebrae are drawn outwards, all of these actions having the effect of increasing the volume of the thorax and hence causing air to pass into the lungs. The action of the external intercostal muscles Mayow understood, and he was under the impression that the internal intercostal muscles had the same effect, viz. the raising of the ribs, and assumed that the two sets of muscles were set in opposite directions in order that they might balance each other, the resultant pull being exerted directly upwards. That a single muscle with a direct upward pull was not in use was explained "quia costarum interstitia adeo minuta sunt ut si muscoli isti rectis angulis insererentur breviores essent quam ipsa musculorum natura patitur".²²⁾

On expiration the muscles relaxed, the ribs sank, and the various parts of the chest were

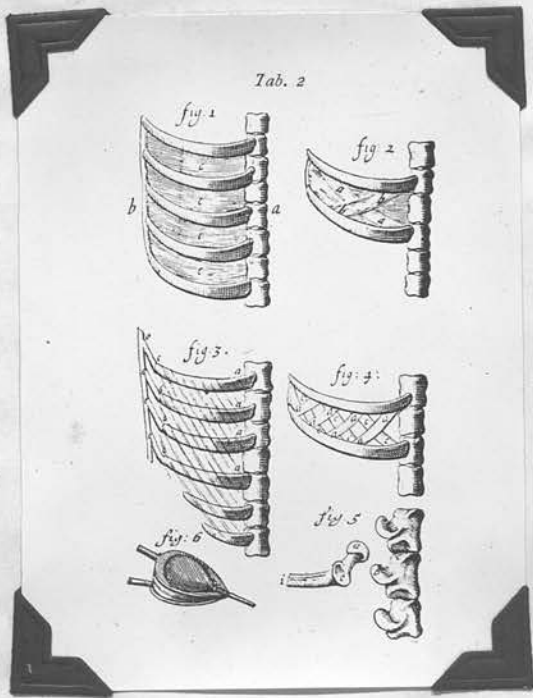


Diagram from Mayow.

restored to their normal positions without the aid of muscular activity. Mayow was of the opinion that the diaphragm was the chief muscle of respiration. On contraction, its curvature became reduced, its dome became flattened, it pressed down the abdominal viscera, increasing the volume of the thorax and causing the intake of air.

"Nempe imprimis assero si superficies sinuata, cuius circumferentia quaquaversum parti immobili affigitur contractionem passa fuerit, eandem circumquaque versus partem immobilem delatum in & superficiem sinuatam versus Planum nunquam vero ultra planum ituram esse" ²³⁾ .

When expiration occurred the diaphragm relaxed, the abdominal viscera pushed it up and the chest volume was diminished. The abdominal muscles also played a part in breathing, especially in forced respiration.

Some of Mayow's experiments were very significant. He found that the lungs collapsed when the chest was opened but that they could be inflated by means of the bellows and that if a

the blood into the air in the tubes and was ex-

constant stream of air were kept passing into the lungs and out of holes pierced in their substance, life was maintained in the animal. Hence the motion of the lungs was not necessary for life nor could their use be the churning up of the blood or its transport from the right side of the heart to the left. Mayow therefore came to the conclusion that a component of the air, the "nitro-aerial spirit" as he called it, passed in the lungs into the blood and was carried thus to the muscles, particularly the heart. When breathing was stopped the supply of "nitro aerial spirit" to the heart ceased, its beating stopped, and death resulted.

"Plane ut praecipuus respirationis usus esse videatur ut musculorum et praecipue cordis motus insutuatur" ²⁴⁾ . Exercise increased the need for "nitro-aerial" spirit in the muscles and hence respiration was augmented.

The fact that an exchange of gases took place in the lungs he did not fully grasp, although he was on the point of doing so. It was left to later men to show that carbon dioxide passed from the blood into the air in the lungs and was ex-

pired.

III. EARLY DISCOVERIES RELATION TO THE GASES INVOLVED IN RESPIRATION.

The fact that the metabolism of living body involves the consumption of oxygen and the production of carbon dioxide has been known for several centuries and a few remarks on the early knowledge of the relationship of these gases to the respiratory process might conveniently be made at this point.

Although Van Helmont (1577-1644) was the first man to use the term gas in the modern sense, Leonardo da Vinci (1452-1519) before him had realised that the atmospheric air had two constituents.²⁵⁾ One of these constituents, oxygen, was investigated by Mayow¹⁷⁾ in 1669 and later by Hales (1731)²⁶⁾ and Bayen (1774) but Joseph Priestly is generally regarded as its discoverer (1774). He, however, was forestalled by Scheele who prepared it in 1772 by heating mercuric oxide and by other methods and who performed many experiments on the effect of respiration on the

composition of atmospheric air. ²⁷⁾ He found that during respiration the oxygen of the air was used up so that if air were breathed over and over again it finally ceased to support life and to maintain the combustion of a candle.

His results were published later, however, than those of Priestley who obtained oxygen in the classical experiment of heating mercuric oxide by means of the sun's rays focussed on it through a magnifying glass. ²⁸⁾ He found that mice lived in this gas for a longer period than in normal air ²⁹⁾. His experiments were repeated in France by Lavoisier whose work on the calcination of mercury is outstanding in the annals of science ³⁰⁾. To him also is due a considerable amount of credit for the discovery of oxygen; "Cet air que nous avons découvert presque en même temps M. Priestley, M. Scheele, et moi a été nommé par le premier air déphlogistique; par le second air empiréal. Je lui avois d'abord donné le nom d'air eminentment respirable depuis on y a substitué celui d'air vital" ³¹⁾. The phlogiston theory to which reference is made above was put forward by

Becher (1669) and Stahl (1721). It assumed that every combustible substance contained a fire stuff - phlogiston-which was lost on combustion and the theory was enthusiastically taken up by many eminent men including Priestley who showed its application to respiration:- "Respiration is a phlogistic process affecting air in the very same manner as every other phlogistic process affects it." ³²⁾

It was Lavoisier who finally overthrew the phlogiston theory by showing that metals increased in weight on burning in air, a conclusion arrived at by Mayow in the previous century. ¹⁷⁾

Carbon dioxide was first discovered in 1757 by Joseph Black ³³⁾ who called it fixed air ³⁴⁾ and later showed that it was a compound ³⁵⁾. Its ³⁶⁾ effect on animals was investigated by Lavoisier who showed that mice when placed in the gas went almost immediately into convulsions whereas when placed in air from which oxygen had been removed, they showed signs of laboured breathing but death was not immediate, nor were the convulsions so severe or so immediately evident.

The effect of respiration on air was studied by many investigators including Boyle, Hales, Black, Priestley, and Lavoisier but chiefly by the last two. ³⁸⁾

Priestley and before him Cigna, Blare, Boerhaave, and Haller examined the effect of air and oxygen on blood and correlated their results with the actions taking place in the lungs during respiration ³⁸⁾. It was shown that blood exposed to oxygen became bright red and to carbon dioxide became black, and these experiments were later repeated by Lavoisier ³⁹⁾ who fully realised that in respiration the oxygen of the air was the only constituent to undergo chemical change, the nitrogen ⁴⁰⁾ passing in and out of the lungs unchanged. He realised also that the oxygen absorbed was converted into carbon dioxide "Si l'en enferme des animaux dans une quantite donné d'air ils y périssent lorsqu'ils ont absorbé ou converti en acide crayeux ⁴⁰⁾ aeriforme, la majeure partie de la portion respirable de l'air et lorsque ce dernier est réduit à l'état de mosette".

His experiments on sparrows were duplicated

on mice by Priestley who also found that
respiration involved the consumption of oxygen and
liberation of carbon dioxide. ⁴¹⁾

Many years before this however Boyle had
investigated respiration and had found that blood
placed in a vessel exhausted of air gave off great
volumes of gas ⁴²⁾. He also investigated the
effect of placing small animals, vipers, frogs,
kittens, mice and birds, in a rarefied atmosphere
and compared these results with the effects
experienced by human beings at high altitudes. ⁴³⁾

IV. THE EIGHTEENTH CENTURY.

Boerhaave whose views were published at the beginning of the 18th century had some original ideas on the subject of respiration and the cause of the contraction of the respiratory muscles.⁴⁴⁾ .

When blood passed from the lungs into the left ventricle, it mounted from there to the cerebellum causing "nervous fluid" to flow to the muscles of inspiration so that they contracted .

After their contraction i.e. at the end of inspiration, arterial blood acted with less force on the muscles so that they were obliged to relax.

During their contraction also, i.e. during respiration, less blood passed to the left ventricle from the lungs and therefore less blood mounted to the cerebellum, and the nervous tension relaxed.

The causes of the contraction of the intercostal muscles being thus diminished, the muscles relaxed and expiration occurred. The idea of a fluid in the nerves was held as late as 1745 by Le Cat⁴⁵⁾ and others.

Mayow's observations were corroborated by Drake in 1702⁴⁶⁾ who sought to disprove the

suggestion by Willis that the external intercostal muscles raised the ribs and the internal intercostals lowered them. He pointed out that since the upper ribs were less movable than the lower ones, the contraction of either set of muscles would cause the latter to rise. He was of the opinion that the abdominal muscles and various other muscles (e.g. serratus anterior) attached to the ribs, did not come into action except in forced respiration.⁴⁷⁾ About the year 1728 Houston performed many experiments on dogs. On making punctures in the chest wall he found that no ill effects were produced and the animals continued to breathe and act normally except in a few cases where the lungs were extruded from the wounds (a tendency in these experiments which had been noted by Highmore¹⁸⁾ and van Swieten⁴⁸⁾), but if a big aperture were made in the chest wall by the removal of portions of the ribs, collapse of the lungs followed⁴⁹⁾. He concluded that in the case of small punctures in the chest wall, on expansion of the chest air entered both at the glottis and at the wounds in proportion to their

size. If the wounds were small there was enough air passing through the glottis to keep the lungs at least partially inflated, enough indeed to maintain life and activity.

Hales made similar experiments to Houston and found that if an opening were made in one side of the chest of a dog, the lung of that side collapsed but the other lung functioned as before and was sufficient to maintain life. On straining, the collapsed lung would dilate and emerge through the wound. 50)

Bertier stated that the lungs might continue to dilate even when the chest was opened. 51)

Houston's observations were later criticised by de Bremond 52) who found that if the chest and lungs were both pierced death soon followed but if the chest alone were pierced life continued almost normally. The movements of the chest and those of the lungs however were not isochronous; the lungs dilated when the chest contracted and vice versa. When a larger opening was made by the removal of portions of the ribs, portions of the lungs were extruded. By pinching the phrenic nerve after opening the thorax he found that there

was contraction of the muscles of the thorax and of the diaphragm and acceleration of the heart. By inflating the lungs he caused a similar contraction of the diaphragm and intercostal muscles. He explained this, however, thus:- "Il y a tout bien de croire que le poumon en se dilatant touchoit ou comprimoit le nerf diaphragmatique". His main conclusions, however, were a little wide of the mark. He stated that in the normal condition the lungs and the chest might contract synchronously but in forced respiration they might contract independently or even contrarily. De Bremond's theories about the functions of the phrenic nerve found expression later in the views of Martine who suggested that at the end of inspiration the inflated lungs pressing upon the phrenic nerve paralysed it so that the diaphragm relaxed producing expiration. 53)

Winslow in 1738 submitted Borelli's work to critical consideration 67) and came to conclusions which were not altogether the same as those of his predecessor. While Borelli had held that the intercostal muscles and the diaphragm acted in

conjunction with one another Winslow held that they were independent. The diaphragm could act alone, the intercostal muscles especially those of the lower ribs maintaining the bones in a firm position for the diaphragm to pull upon when contracting which it did by flattening out its arch, the central tendon remaining fixed. Among the muscles of inspiration he included the scalene muscles and the serrati posteriores superiores as well as the intercostals, both sets of which he considered to have the same action viz. the raising of the ribs. He emphasised the obliquity of the ribs and also their double articulations especially the articulations of the first pair which were firmly attached to only one vertebra (1st dorsal). Their firm attachment to the sternum, also, rendered impossible their movement independent of that of the vertebra so that they could therefore act as a fixed base to which the other ribs could be drawn up on contraction of the intercostal muscles.

In 1729 Senac⁽⁶⁸⁾ published some observations on the diaphragm . He came to the conclusion

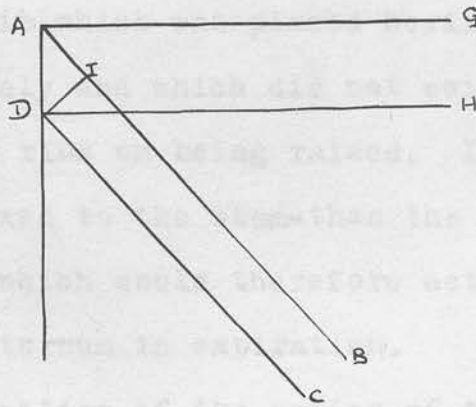
that the diaphragm was not necessary for respiration though, as a rule, it was in action, helping the intercostal muscles. Their action in raising the ribs, however, was opposed by the diaphragm which tended to draw them downwards and inwards.

By cutting the phrenic nerve, he prevented the diaphragm from contracting and found that the lower ribs were pulled upwards and outwards. He decided therefore that the use of the diaphragm was twofold

- 1) on contraction it flattened and so aided respiration by expanding the thorax.
- 2) it kept the lower ribs in check when they tended to be pulled upwards and outwards by the intercostals.

69)
Senac in 1724 drew attention to the apparent paradox that when the intercostal muscles contracted the ribs were not approximated but moved further apart, and he explained this by pointing out that the vertical distance DI between two oblique ribs AB and DC was less than the vertical distance DA between two horizontal ribs

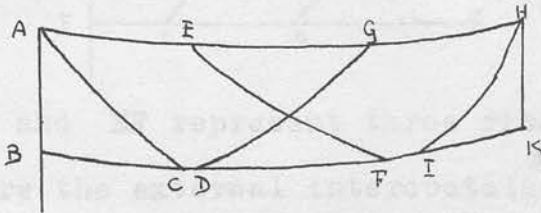
AG and DH.



He also rejected the theory that the internal intercostal muscles served for expiration and stated that if the fibres joining two ribs contracted, no matter what their direction, the more movable (i.e. lower) ribs would be drawn towards the less movable i.e. upper ribs. He found that the intercostals and the diaphragm were the only muscles of respiration though the triangularis sterni muscle might help in expiration by approximating the rib cartilages and so lowering the ribs. Faced with the difficulty that if the intercostals contracted at the same time as the diaphragm the action of the one in raising the sternum would oppose the action of the other which would tend to lower it, he explained this by proving that the central tendon

remained fixed while the rest of the diaphragm contracted. He showed the importance of the position of the first rib which was placed horizontally and not obliquely and which did not swing outwards like the other ribs on being raised. It was more firmly fixed to the sternum than the other ribs by its cartilage which could therefore act as a spring lowering the sternum in expiration.

His explanation of the action of the intercostal muscles was as follows:-



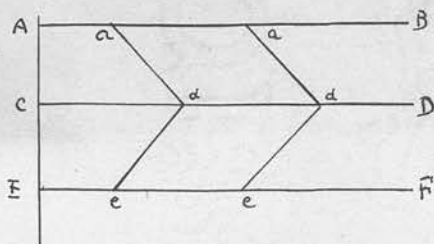
AB represents the back-bone and HK the sternum while AC and EF represent the external and HI and GD the internal intercostals. The fibres AC and HI have the same action and when they contract, the points A and H being fixed the rib CDFIK must rise. The same argument also applied to the fibres EF and GD. Both sets of intercostals had therefore, in Senac's opinion, the same action.

Gibson⁷⁰⁾ and Winslow⁷¹⁾ also stated that

the internal intercostals raised the ribs in the

same way as the external intercostals.

The other side of the question of the use of the internal intercostal muscles was taken up by Swammerdam¹⁰⁾ and Bayle and after them by Hoadly⁷²⁾ who held that the internal and external intercostals were antagonistic. Hoadly's argument is this:-



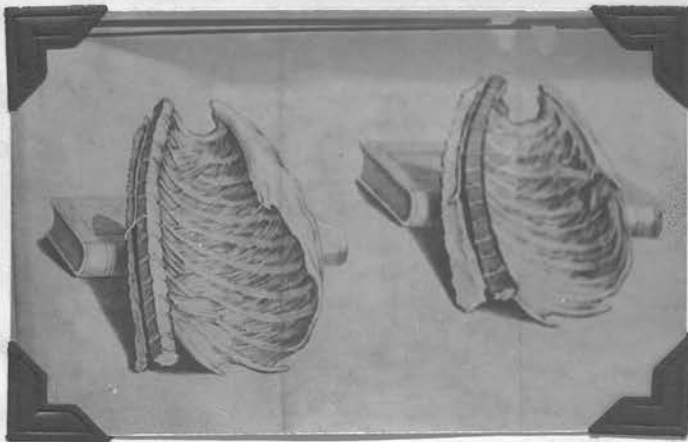
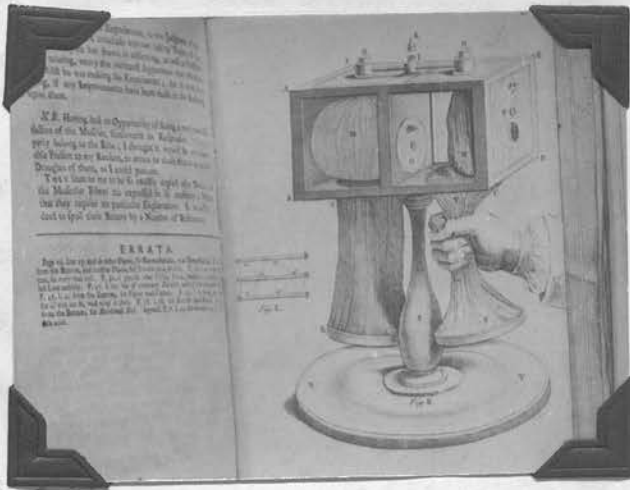
AB CD and EF represent three ribs between which are the external intercostals^{ad} and the internal intercostals ed ACE are the fixed ends of the ribs.

If ad shorten CD will rise

If ed " " " fall

ad cannot shorten unless ed lengthens and vice versa.

If both shorten CD will remain fixed. Similarly if all the external intercostals shorten the ribs will rise and if all the internal intercostals shorten the ribs will be depressed except the lower



Diagrams from Hoadly.

ones which ^{are} held fast down by the serratus posterior inferior. " Since then these ranges cannot both be contracted at the same time; and when they contract separately one set elevates and the other depresses the ribs; is it not highly reasonable to conclude that they were designed by Nature to act separately and successively to each other? "

Hoadly also performed several experiments upon dogs and found that on making a fairly large aperture in the chest a violent dilatation of the lungs occurred, followed by the protrusion of a considerable amount of their substance, and from this and other considerations came to the conclusion that the cavity of the thorax contained air which played an important part in the inflation and deflation of the lungs, and that the thorax did not enlarge so as to contain the inflated lungs but to rarify the enclosed air and diminish the pressure on the external surfaces of the lungs. [One of the greatest physiologists of the 18th century was Haller and we must at this point consider his views on respiration ⁵⁷⁾. Air, he stated, entered the lungs since, on expansion of the thorax, the air



Portrait of Haller.

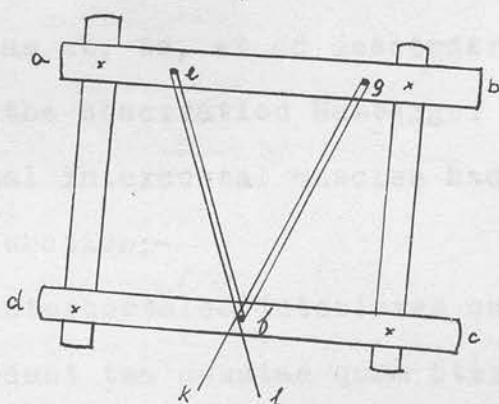
in the lungs became rarefied and therefore had a smaller pressure than the atmospheric air which consequently rushed in. The expansion was brought about by the action of the intercostal muscles ⁵⁸⁾, both internal and external, which pulled the ribs upwards, thrusting the sternum upwards and forwards, and so increasing the circumference of the thorax. The greatest share of inspiration however was taken by the diaphragm ⁵⁹⁾ which on contraction depressed the abdominal viscera and increased the perpendicular diameter of the thorax. Normal breathing, in fact, was brought about mainly by the diaphragm. Expiration was brought about by the muscles of the abdominal wall. The recti muscles on contraction compressed the bulging abdominal viscera, forcing the diaphragm up and causing the volume of the thorax to be diminished. The oblique muscles compressed the sides of the abdomen and in addition drew down the ribs, while at the same time the transverse muscles compressed the viscera and pulled the ribs cartilages inward. By means of all these actions the capacity of the thorax was diminished, and

this together with a contraction of the musculature of the bronchi and bronchioles caused expulsion of air from the lungs.

In forced respiration, inspiration might involve many extra muscles, especially those attached to the ribs, clavicle or scapula while expiration involved the muscles of the back and loins. While Haller's main conclusion was that normal inspiration was brought about by the diaphragm and expiration by the muscles of the abdominal wall, he hinted however that this was not all:- "It is by some queried whether or no there are not other causes of alternate respiration? Whether or no we may hope for any discovery in this matter by compressing the *vena azygos*, the phrenic nerve, or intercepting the blood sent to the brains." ⁶⁰⁾ Haller ⁶¹⁾ and Mayow ⁶²⁾

before him put as evidence of the use of the internal intercostal muscles in inspiration the fact that in the dead body the thorax was found to be expanded with these muscles in the contracted condition. This and other evidence he brought forward in his "de Respiratione experimenta" ⁶⁴⁾

in which he engaged in fierce controversy with
 Hamberg⁶³⁾ who was one of the staunchest up-
 holders of the view that the internal intercostal
 muscles had an expiratory function. In order to
 explain the action of these muscles Hamberg used
 a model which has now become famous.



ab, dc, ad, bc, are four rods fastened together
 by loose pins at a, b, c, d, so that movement is
 possible at the junctions. ab and dc represent two
 adjacent ribs, ad represents the backbone, and bc
 the sternum. f is a pin from which threads pass
 over the pins e and g to l and k respectively so
 that a pull at k represents the contraction of the
 internal intercostal and a pull at l the con-
 traction of the external intercostal. The action
 is explained by Hamberg as follows:-

"quod si igitur globulo f annectatur filum, istud-

que circa globulum e voluatur et rursus in f firmetur, regula vero ad manu teneatur, et filum constringatur, videbis omnes reliquas tres regulas ascendere, tametsi superiorem deorsum trahis: quod si vero idem filum globulo f connexum voluas circa globulum g in globulo f denuo finnes et filum constringas, videbis in utroque casu tres regulas ab, bc, et cd descendere."

From the observation Hamberger concluded that the internal intercostal muscles had an expiratory function:-

"Musculi intercostales interiores quando agunt.

- 1) descendunt tam coastae quam sternus postito hoc elevatur fuisse.
- 2) sterni distantia a vertebrae fit minor.
- 3) cavitas thoracis angustatur, vi contrariorum diaphragmatis.
- 4) costarum distantia inter se fit minor et fibrae musculi intercostalis exterioris extenduntur."

The controversy between Haller and Hamberger was long and sometimes bitter but the precise action of the internal intercostals remained doubtful for many years and can hardly be said

to be conclusively settled even at the present day. [Zinn about 1755 performed some important experiments in the nervous mechanism of respiration. 65) In the brain of a dog he made an incision passing through the cerebellum and the fourth ventricle. Eight hours later the heart was still beating and respiration was continuing.

On opening the chest and applying pressure to a point on the phrenic nerve he found that if the nerve was irritated above the point, there was no result but if irritated below, contraction of the diaphragm occurred.

His experiments were corroborated by Haller 66) who found that stimulation of the phrenic nerve or its distal end if cut, produced contraction of the diaphragm. [De Bremond's work, in turn, came in for criticism, especially by Whytt 54) who was severely opposed to de Bremond's view that the lungs were capable of expansion on their own account. He also subjected the views of Boerhaave and Martine to careful criticism.

It is in the writings of Whytt that we first begin to see glimpses of the modern theory of

respiration ⁵⁵⁾. Here the suggestion is made of a stimulus arising on the lungs. The blood passing through the lungs found its course most impeded at the end of expiration. It therefore distended the pulmonary vessels thus stimulating the pulmonic nerves and causing the contraction of intercostals and diaphragm. As the result of inspiration the blood found an easier passage through the lungs, the stimulus was removed and the muscles relaxed, causing expiration. Whytt realised also that the pulmonic plexus had no direct nervous connection with the phrenic nerve but that the two were connected through the medium of the brain and hence that respiration was under the control of "some percipient being" as he puts it.

"We are not to ascribe this to any unknown sympathy acting mechanically upon these muscles or their nerves; but to the MIND or sentient principle, which being affected by the uneasy

perception in the lungs, is thereby excited to determine the influence of the nerves more copiously into the intercostal muscles and diaphragm".

Expiration, he considered to be due to the return of the various parts to their normal positions under their own elasticity, although the abdominal muscles might be affected by a slight stimulus.

The influence of the mind over respiration is emphasised by Whytt. He pointed out that the stimulus passing up from the lungs was so weak that it was easily obliterated by the will, so that the respiration movements could be voluntary—we could alter or stop our breathing at pleasure. The fact that respiration continued during sleep did not disprove that it was under the control of the will. So a slight indeed were the stimuli passing up from the lungs that other stimuli might easily overpower them, e.g. surprise stopped hiccup, deglutition lessened fits of coughing, sneezing was stopped if it caused pain and so on.

Although Whytt's work is of great importance it does not appear to have received due recog-

nition by later physiologists. [About the same
 time Hartley seems to have had similar but less
 clearly expressed ideas. 56)

"It may be supposed that the diaphragm and
 intercostal muscles are as it were fatigued by
 constant action; and that they incline to
 sympathise in inactivity with the rest of the
 muscles, especially during Sleep. But then the
 Accumulation of Blood in the Lungs, which the
 Intermission of Respiration must be occasion after
 it has once had a free Passage through the lungs
 by means of Respiration will produce so much
 uneasiness in the lungs and particularly in their
 external Membrane which is continuous to the
 pleura, as will renew respiration."

V. THE NINETEENTH CENTURY AND ONWARDS.

At the beginning of the nineteenth century Magendie ²³⁾ summed up the controversies of previous years in these words - "Rien n'est plus simple à concevoir que le mécanisme de ce mouvement, des que la disposition physique des parties est bien connue; et cependant il a été l'object de discussions très vives entre des auteurs estimables, qui ont donné à cette question une importance que peut-être elle ne méritait pas."

He goes on to criticise Haller's opinions especially his view that the first rib was the least movable of all. Magendie held that simple observation and also examination of the articulations of the ribs showed that the first rib was most movable and that the ribs became less so passing downwards. He also stated that the ribs were raised and lowered not by the action of the intercostal muscles but by the action of the muscles which attached them to the vertebral column. [Another worker at the beginning of the nineteenth century was Bell who in 1821 published

the results of his observations on the respiratory nerves among which he included the vagus, spinal accessory, external respiratory (long thoracic), phrenic, and the "portio dura" of the seventh. On this last he laid great stress since some of its fibres passed to the nostrils, the movements of which could be used as a measure of the force of respirations ⁷⁴⁾. He utilised this in an experiment upon an ass in which the phrenic nerves were divided to stop the action of the diaphragm and the spinal cord severed below the cervical vertebrae to stop respiration in the chest. There remained strong action in the muscles of the face and nostrils showing that ineffectual endeavours were being made to carry on respiration, endeavours which eventually ceased but were restored on the application of artificial ⁷⁶⁾ respiration.

Bell pointed out ⁷⁵⁾ that most muscles of respiration were supplied by two sets of nerves, respiratory and voluntary, and recorded, among others, a case of complete hemiplegia in which the voluntary ~~nerves~~ to the shoulder muscles were paralys-

ed while the respiratory nerves still functioned. He also recorded that respiration could be stopped or at least interfered with by injury to the vagus nerve (a fact observed by Haller and others) and also by injury to the medulla oblongata from which most of the respiratory nerves arose.

The Respiratory Centre.

Perhaps the most noteworthy work on the subject of respiration which was done during this century was the investigation and location of the respiratory centre. While the name of Flourens is generally associated with its discovery, several men before had postulated its existence and had had even roughly defined its position.

Lorry⁷⁸⁾ noticed that respiration ceased immediately on the severance of the spinal cord between the second and third cervical vertebrae, but Le Gallois went very much further. He noticed that decapitation affected respiratory movements⁷⁷⁾ more than other movements, and suggested the existence of a respiratory centre situated in the medulla oblongata close to the foramen magnum near the origin of the eighth pair of nerves (vagi) -- "le lieu où réside dans la

moelle allongé le premier mobile des phénomènes
 mecaniques de la respiration embrasse l'origine
 des nerfs de la huitième paire." A cut through
 this point involving the origin of the eighth
 nerves caused immediate cessation of respiration. ⁷⁹⁾

He also devised and described a pump (Fig. [])
 which he used in the maintenance of artificial
 respiration. ⁸⁰⁾

In 1824 Flourens published his observations
 on the nervous mechanism of respiration and these
 were of the greatest importance. He found ⁸¹⁾
 that injury to the brain above the medulla oblongata
 had little or no effect on respiration but that
 injury to the medulla oblongata itself caused
 immediate cessation of breathing. Destruction
 of the spinal cord below the origin of the last
 pair of intercostal nerves had no effect on
 respiration but if the cord were gradually destroy-
 ed from that point upwards respiration became more
 and more difficult as the intercostal muscles were
 thrown out of action, and when the origin of the
 phrenic nerves was reached respiration ceased
 entirely save for the movement of lips and nostrils
 mentioned by Bell.

Movements divided into three classes -
four classes.

- (1) The Quantity of the movement of the...
- (2) The Quality of the movement...
- (3) The direction of the movement...
- (4) The position of the...

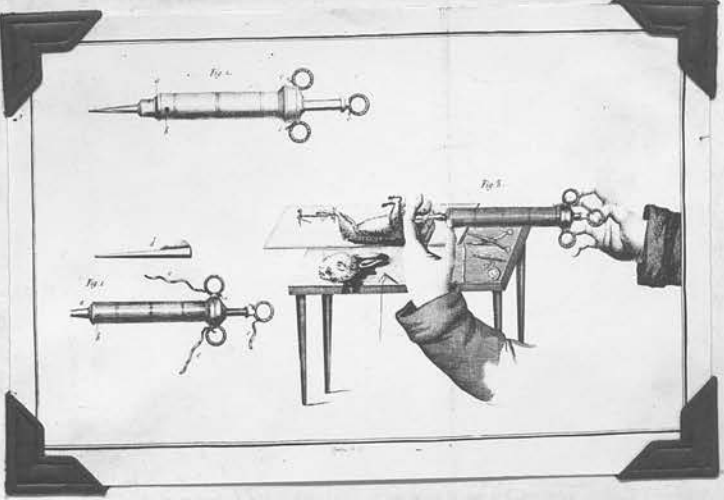


Diagram from Legallois.

Fig 1

Flourens divided respiratory movements into four classes

- (1) The Opening of the nostrils or mouth.
- (2) The Opening of the glottis.
- (3) The raising of the ribs and shoulders.
- (4) contraction of the diaphragm.

The second could be stopped by destroying the origin of the eighth pair of nerves, the third by destroying the costal portion of the spinal cord, and the fourth by destruction of the origin of the phrenic nerves. To destroy the first he sliced off the medulla oblongata from before backwards until dilatation of mouth and nostrils first disappeared leaving the inspiratory movements of the trunk unaffected. Piercing the medulla oblongata a short distance above the origin of the eighth pair of nerves produced no effect on respiration but below this level Flourens stated that there was some point which controlled respiration - "Nul de ces mouvements ne contient en soi le premier principe de son action. Il suffit de les isoler d'un point donné pour qu'aussitot ils s'éteignent; il suffit de les maintenir réunis à ce point, pour qu'ils se conservent: c'est donc évidemment de ce

point, et de ce point seul qu'ils tirent leur premier mobile".

This point acted as chief regulator of respiration and through the spinal cord it controlled respiratory movements. But not only did the medulla oblongata act as regulator and excitor of respiratory movements, it acted also as their producer, especially in the case of fish where it was the exclusive organ of the respiratory mechanism. This view did not altogether meet with the approval of other physiologists. Marshall Hall⁸³⁾ for example looked upon the medulla oblongata as combining the action of the different muscles into the acts of respiration and considered respiration to consist of excited acts, the excitor nerves being the fifth, pneumogastric, and spinal nerves. He viewed "the respiratory as but a part of a more extensive system - as an excited and not a spontaneous function - as originating when the cerebrum is removed in the pneumogastric as its excitor and not in the medulla oblongata."

Flourens also attempted accurately to locate the centre by making transverse slices through the medulla oblongata in the rabbit.⁸²⁾

He found that the centre lay at the level of the origin of the eighth (pneumogastric) pair of nerves and extended downwards for a very short distance. A cut through the centre caused immediate cessation of respiration, a cut immediately above it did not affect respiratory movement in the trunk and a cut immediately below it did not affect respiratory movements in the head. Although injury to this vital part of the medulla oblongata caused such immediate and lasting results he removed the cerebral hemispheres, the corpora quadrigemina and the cerebellum without causing complete stoppage of breath - an experiment similar to some performed later by Rosenthal. Although Flourens tended to limit the respiratory centre to a rather circumscribed point, later observers did not confirm it to such narrow limits. Some including Brown Séquard, Langendorff and Wertheimer even described respiratory centres in the spinal cord, but most investigators agreed that the centre was bilateral since the movements of respiration were little affected by a longitudinal section in the middle line of the medulla oblongata.

84)
Gierke in 1873 stated that in the rabbit the centre extended from a point 3 or 4 mm. in front of the calamus to a point 3 or 4 mm. posterior to it, the situation corresponding to that of the solitary bundle, and Martin and Booker⁸⁵⁾ in the same animal found a centre for respiration close to the iter underneath the posterior corpora quadrigemina, stimulation of which caused acceleration of respiration.

86)
Mislowsky stated that the centre lay near the middle line in the formatio reticularis while Gad⁸⁷⁾ described it as a relatively large area in the lateral portion of the formatio reticularis.

88)
Lewandowsky showed that no changes in respiratory movements occurred when sections were made through the mid brain without removal of the posterior corpora quadrigemina. On their removal respiration became slow and inspiration prolonged.

Rosenthal found that rhythmical respiratory movements continued after section of the posterior roots of all the cervical spinal nerves, section of the spinal cord at the seventh cervical vertebra, section of the vagi, and section of the brain

at the corpora quadrigemina cutting off all impulses from the higher centres. The medulla oblongata was thus isolated from all impulses except those from the fifth, seventh, eighth, and ninth cerebral nerves and the fact that rhythm was still maintained suggested automatism of the centre.

89) Brown following up the observations of Markwald came to the conclusion that a centre for the control of respiration existed in the mid brain at a point 3 mm. to the side of the aqueduct. Stimulation of this point gave rise to gasping movements although stimulation of the area circumscribing the point was ineffective.

Lewandowsky's results were verified by 90) Trevan who suggested that the centre was a chain of neurones running along the floor of the fourth ventricle and into the iter.

91) In 1919 Barcroft concluded that the respiratory centre was intrinsically rhythmic but that impulses in the nerves passing to it might modify the rhythm. Some of the most 92) recent work on this subject was done by Lumsden

93) who maintained that only one centre existed.

who divided the respiratory centre into three regions:

(1) a gasping centre below the ~~striae~~ ^{striae} ~~acousticæ~~ ^{acousticæ}

(2) an apneustic centre at the level of the ~~striae~~ ^{striae} ~~acousticæ~~ ^{acousticæ}, whose impulses caused prolonged inspiration.

(3) A pneumotaxic centre in the upper pons region which produced normal respiration by inhibiting the apneustic centre.

Further investigation ⁹³⁾ led him to include an expiratory centre just below the level of the ~~striae~~ ^{striae}, this centre also being controlled by the pneumotaxic centre.

These centres were controlled ⁹⁴⁾ by three factors

(1) Chemical - excess of carbon dioxide and lack of oxygen in the blood.

(2) Nervous impulses chiefly from the vagus nerve.

(3) Impulses from higher centres as in voluntary respiration.

Lunsden's views were however criticised by Huggett and Mellanby who maintained that only one centre ⁹⁵⁾ existed.

The question of the excitability of the respiratory centre and its variations with the composition of the blood has been the subject of much controversy and much investigation particularly by Haldane and his collaborators.

Lumsden's view ^{93 & 94)} is that hydrogen ions in the blood "increase the excitability of the pneumotaxic centre so that it periodically discharges and inhibits the tonic apneusis and thus in conjunction with the vagus determines the rhythm of respiration of normal type" ⁹⁶⁾.

He considered that carbon dioxide stimulated the apneustic centre, and when present in excess, the expiratory centre. Should the excess of carbon dioxide not be diminished, the pneumotaxic centre became more excitable causing greater ventilation which stimulated the vagus endings in the alveoli more powerfully than usual so that breathing was still further accelerated by vagus action, but even with the vagi cut the increased hydrogen ion concentration and excess of carbon dioxide would be sufficient to accelerate respiration. Lack of oxygen, in Lumsden's opinion, had no effect if

small but should it be great, apneusis would be stimulated. Very great lack of course would lead to death by asphyxia.

While it is now generally agreed that excess of carbon dioxide is the important factor in the stimulation of the centre, among the physiologists of a few years ago there was much difference of opinion.

Some including Marshall Hall, Valentin,⁹⁷⁾ Traube, Zuntz⁹⁸⁾ and Friedländer and Herter held that the presence of excess carbon dioxide was the important factor while others including Rosenthal, Pflüger,⁹⁹⁾ Vervorn, Bethe¹⁰⁰⁾, Zuntz and Loewy¹⁰¹⁾, and Hill and Flack¹⁰²⁾ stressed the part played by low oxygen tension. Winterstein¹⁰³⁾ held that hydrogen ion concentration was the main factor and that carbon dioxide had no specific effect. It was however, through the researches of Haldane and his co-workers that most light was thrown on this subject.

In 1892 Haldane and Lorrain Smith¹⁰⁴⁾ found that hyperpnoea was due to excess of carbon dioxide and was but little affected by deficiency

of oxygen unless that deficiency were great. This view was reiterated by Scott ¹⁰⁵⁾ who stated that the respiratory centre was stimulated by slight amounts of carbon dioxide or by great diminution of oxygen pressure in the inspired air.

Orr and Watson ¹³⁰⁾ found that in the duck carbon dioxide in the inspired air inhibited respiration while lack of oxygen produced excitation.

In 1904 Haldane and Priestley ¹⁰⁶⁾ confirmed the work of Miescher ¹³¹⁾ and stated that the centre was excited by a very small increase of alveolar carbon dioxide pressure and by considerable lack of oxygen - the former being the main factor. They found that apnoea depended on the fall of carbon dioxide pressure if the oxygen pressure were still sufficiently high not to cause excitation.

Hill and Flack ¹⁰¹⁾ on the other hand came to the conclusion that diminished oxygen tension was the most potent factor in the regulation of respiration during obstructed aeration although in muscular exercise excess of carbon dioxide was most effective.

Haldane and Poulton (107) stated that if the oxygen pressure in the inspired air were decreased it was not the lack of oxygen that stimulated the centre but the presence of carbon dioxide, the action of which was still further augmented by the increased acidity of the blood produced by the want of oxygen. They also pointed out that if oxygen lack were gradually produced there was no great hyperpnoea since the carbon dioxide had time to be gradually removed. (108) Douglas and Haldane showed that lack of oxygen would excite the centre probably by permitting the formation of lactic acid, but that during muscular exercise it was the rise of carbon dioxide pressure which caused stimulation, again possibly by the formation of lactic acid, the consequent increase in the acidity of the blood causing increased excitability of the centre.

The Nervous Control of Respiration.

So much work has been done on this subject of recent years that it would be impossible to give a comprehensive survey of it here. It must suffice if in this essay we give but a brief summary of the main conclusions reached by the



foremost investigation in the field. The effect of severance of the vagus nerve on respiration had been known for centuries but the precise significance of this nerve in normal respiration was first made plain in 1868 when Hering and Breuer published the results of their investigations. ¹⁰⁹⁾

They realised that the vagus nerve was continuously carrying impulses from the lungs to the medulla oblongata and that these impulses were of two kinds, inspiratory (excitatory) impulses from the empty lung and expiratory (inhibitory) impulses from the distended lung.

Traube showed that cutting of the vagus caused respiration to become slower and that stimulation of the central end caused acceleration of respiration owing to the excitatory fibres being more easily stimulated than the inhibitory. ¹¹⁰⁾

These impulses which are passing from the lungs in the vagus with each respiration can be demonstrated with the string galvanometer.

Lewandowsky ¹¹¹⁾ first showed that there was a negative variation in the demarcation current from the peripheral end of a divided vagus on

expansion of the lungs. Alcock and Seeman

122 & 133)

also found that impulses travelled in the vagus during breathing and concluded that distension or collapse of the lungs excited the vagus endings.

Einthoven performed many experiments on electric currents in nerves and found action currents in the vagus with each inspiration, and Winterstein curarised an animal to eliminate the action of the respiratory muscles, divided the phrenic nerve, connected the central end with a galvanometer, and found that rhythmic currents were registered showing that the centre was sending out rhythmic impulses which were independent of the contraction of the respiratory muscles.

144)

115)

The vagus is undoubtedly the most important nerve in the regulation of respiration but Boruttau showed that impulses from active muscles might affect respiratory movements.

116)

The action of the vagus was investigated by Loewy who found that expansion of the lungs stimulated the sensory fibres and quickened the respiratory rate, and by Markwald and Lewandowsky who found that the vagus had a continuous effect on the respiratory centre.

117)

178)

119)

Knoll ¹²⁰⁾ found that expiratory stimuli were produced if the cut end of the nerve fell into the wound in the neck or if it were moistened with saline solution.

By these experiments and by many others it was proved that there were two sets of fibres in the vagus - inspiratory and expiratory but in the investigation of the nerve many difficulties of technique were encountered.

The problem of rendering the vagus non-conducting without at the same time causing stimulation was overcome by Gad ¹²¹⁾ who devised the method of freezing the nerve, a process which prevented the passage of impulses while leaving the nerve undamaged.

In 1889 Head ¹²²⁾ published the results of his extensive experiments on the mechanism of respiration. To obtain records of respiratory movements he exposed and isolated the small slip of the diaphragm attached to the ensiform cartilage in the rabbit and connected it to a lever writing on a smoked drum. Using this method of recording he tried the effect of dividing (freezing) one vagus nerve and obtained an increase in strength and duration/

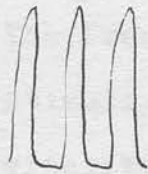
duration of the inspirations, and sometimes a shortening of the expiratory period together with a certain amount of tonic contraction, but after a short time these effects gradually wore off and breathing returned again to normal. If the other nerves were now divided the same changes again occurred but in a more pronounced form. The vagi therefore normally exerted an influence on breathing and their division produced an inspiratory effect. The stimuli passing up the vagi were caused by the expanded or contracted condition of the lungs since closure of the trachea at the end of inspiration caused a decrease in respiratory activity of the centre and a pause followed which was broken by an inspiration, while closure of the trachea at the end of expiration caused an increase in inspiratory activity. Also on inflating the lungs there was a decrease in inspiratory activity and a long pause followed which was finally broken by an inspiration, and removal of air from the lungs caused an increase in the inspiratory activity of the centre. Increase in the volume of the lungs therefore

tended to inhibit respiratory movements while decrease in the volume had the opposite effect of exciting respiration.

Head also investigated the effect of pumping air into or out of the lungs. Positive ventilation or periodic inflation of the lungs resulted in a gradual decrease of respiratory movements and a pause during which the muscles remained relaxed i.e. in the condition for expiration. Negative ventilation or periodic deflation of the lungs resulted likewise in a gradual decrease of respiratory movements followed by a pause during which the muscles of inspiration remained in the contracted condition. (Fig 2)

The action of the vagi was summed up by Head in these words - "During normal breathing the activity of the vagi produces two results - firstly the inspiratory activity of the centre is regulated by the constant inhibitions produced by the dilatation of the lungs and secondly the potential energy of the centre is raised."

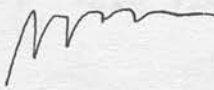
In normal breathing the vagi exercised a two-fold action



Normal Breathing.



Positive Ventilation.



Negative Ventilation.



Compound Ventilation.

From Head, Journal of Physiology Vol. 10.

Fig. 2

- (1) The stimulus from the dilated lung checked the inspiratory contraction when it had reached a certain height.
- (2) The frequently repeated inhibitory stimuli increased the inspiratory vitality of the centre.

Scott¹⁰⁵⁾ regarded the vagi in respiration as similar to the sensory nerves of muscle. He found that with the vagi intact inflation of the lungs even in dyspnoea led to inhibition of inspiration. This was not the case with the vagi cut.

Auer & Meltzer¹²³⁾ showed that the vagus contained expiratory and inspiratory fibres, the former requiring stronger stimuli than the latter, and that when both were simultaneously stimulated expiration predominated during stimulation and inspiration afterwards.¹²⁴⁾ They found also that increasing the pressure of the ingoing air stream during intra-tracheal insufflation caused an expiratory standstill. This effect was absent with the vagi cut. They considered this method an improvement on that of Hering and Breuer inasmuch as ventilation was complete during the standstill

while the earlier observers had clamped the trachea and so stopped ventilation.

Barry¹²⁵⁾ came to the conclusion that inspiratory impulses arose in the thoracic wall and travelled by the somatic nerves and spinal cord to the centre, the impulses travelling by the vagus being chiefly inhibitory.

The Intercostal Muscles.

Little work has been done within recent years on the vexed question of the action of the internal intercostal muscles but such investigations as have been carried out have been of great interest.

In 1879 some important results on the function of the internal intercostals were published by Martin and Hartwell¹²⁶⁾. They pointed out that to determine the action of the internal intercostals by observing rib movements after removal of other muscles might lead to wrong conclusions since muscles which held fast either the upper or the lower of the pair of ribs under examination would no longer be performing their normal functions. To stimulate the muscles electrically also might yield erroneous conclusions unless the other

muscles which normally co-operated with the intercostals were acting in proper order and degree. These investigators therefore exposed the internal intercostals in a dog (or cat) in which artificial was maintained. When this was stopped it was found that during respiratory movements the internal intercostals contracted alternately with the diaphragm. It was therefore concluded that these muscles had an expiratory function. These results were verified by Hough. ¹²⁷⁾

In 1925 Schafer and Macdonald ¹²⁸⁾ isolated a complete hoop consisting of two adjacent ribs and cartilages and the intervening muscles in an animal kept alive by positive ventilation, leaving the attachments to the spine intact. On diminishing artificial respiration the hoop on inspiration moved forward and on expiration backward. The intercartilaginous muscles were found to contract on inspiration and relax on expiration. When these muscles were cut, the external intercostals were able to cause the inspiratory movement, even against the opposing elasticity of the internal intercostals. These investigators were unable to detect any contraction of the latter muscles during

rib depression.

The intercostal muscles however are but little used in normal respiration which is carried on mainly by the diaphragm although costal respiration is noteworthy in women. Investigation shows that this is due rather to constriction of clothing than to any peculiarity of the anatomy and physiology of the female body. Sewall and Pollard¹²⁹⁾ quoting Hutchison, Rosenthal, Mayo and Kellogg, stated that in men respiration was chiefly abdominal, in women costal, although in primitive tribes where civilised dress was not worn respiration was chiefly abdominal in women.

And so we must draw to a close, We are **conscious** of many faults and many errors both of omission and of commission. **Amidst** the vast literature on the subject we have been able to consult only those **works** and those papers which have combined importance with accessibility. We are aware that many investigators and their work have not been mentioned, but if in tracing the course of our knowledge of this subject we have given some idea of the trend of thought during the various

centuries and some account of how earlier work has led up to the knowledge of modern days however brief our survey of that knowledge may be, we shall feel that the purpose of this essay has been at least in part fulfilled and that our work has not been altogether in vain.

- FOSTER - Lectures on the History of Physiology.
- MAYLIS - Principles of Human Physiology.
- STARKES - Principles of Human Physiology.
- PATTERSON - John Hayon in Contemporary Setting.
- SILVER - Chayde Stakes Respiration.

II. PARTICULAR.

- (1) VERMILION Opera Anatomica 1725. Pars 3a. Caput 3. Almond 1. 432.
- (2) HAMILTON De respiratione et eius instrumentis.
- (3) HAYON Anatomie des animaux de la classe des mammiferes en ce qui concerne la respiration et la circulation du sang.
- (4) BROWN Medulla Christiana. 1781.
- (5) BOYLE De respiratione 1662.
- (6) VAN HELMONT Oratio Medicinaria 1668.
- (7) HALLER De Motu Animalium 1746 P. 101 De Motu Respirationis.

BIBLIOGRAPHY.

NOTE: The dates given in the following Bibliography refer to the edition of the work which was consulted in the preparation of this essay and not necessarily to the first edition.

I. GENERAL.

- FOSTER - Lectures on the History of Physiology.
BAYLISS - Principles of General Physiology.
STARLING - Principles of Human Physiology.
PATTERSON - John Mayow in Contemporary Setting.
Gibson - Cheyne Stokes Respiration.

II. PARTICULAR.

- (1) VESALIUS Opera Anatomica 1725
Cura Boerhaave &
Albini P. 492.
(2) FABRICIUS De respiratoione et
eius instrumentis.
(3) HARVEY Exercitatio anatomica
de motu cordis et
sanguinis in animalibus
1628.
(4) SERVETUS Restitutio Christian-
ismi 1553.
(5) COLUMBUS De Re Anatomica 1559
(6) VAN HELMONT Ortus Medicinae 1648.
(7) BORELLI De Motu animalium
1710 P. 102 De Motu
respirationis.

- (8) VESALIUS Fabrica Humani
Corporis 1543.
- (9) STENSEN Elementorum
Myologiae Specimen
1667.
- (10) SWAMMERDAM Tractatus Physico-
Anatomico Medicus de
Respiratione usuque
Pulmonum 1679
Sectio Prima.
- (11) BOYLE Philosophical
Transactions 1670
Vol. 5 P.2043 et seq.
- (12) HALE'S Haemastatics P.83
1732.
- (13) HOOKE Phil. Trans. Vol.2
P.593, 540.
- (14) LOWER Tractatus de Corde
1669 Cap.III De
Motu et Colore san-
guinis.
- (15) LOWER Phil. Trans. Vol. 1
& 2 P. 554.
- (16) MALPIGHI Opera P. 133 et
seq. 1686 De
Pulmonibus (Letters
to Borelli).
Structure of Lungs
Phil. Trans. VI,
1669 P. 2149.
- (17) MAYOW Untersuchungen über
den Salpeter und den
salpetrigen Luftgeist
das Brennen und das
Athmen (Ostwald's
Klassiker No.125).

- (18) HIGHMORE Corporis Humani
Disquisitio
Anatomica 1651 P.180
De Usu et Motu Pul-
monum.
- (19) SPIGELIUS De Humani Corporis
Fabrica. 1699 p.283.
- (20) SYLVIUS Opera Medica 1680.
Experimentum circa
respirationem in
cane factum P. 34.
De Respiratione
usuque Pulmonum
P. 30 et seq.
- (21) MAYOW Medico Physical
Works. Alembic
Club Reprints No.17.
- (22) MAYOW Tractatus Quinque
1674 De Respiratione
P. 282.
- (23) IBID. P. 306.
- (24) MAYOW Tractatus Quinque
1674. Tractatus
Quartus - De Motu
musculari et
spiritibus animal-
ibus. P. 85.
- (25) KENDALL Smith's Inorganic
Chemistry P. 86.
- (26) HALES An attempt to
analyse the air.
- (27) SCHEELE Chemische Abhandlung
von der Luft und
dem Feuer. 1777.
- (28) PRIESTLEY Experiments and
Observations on
different kinds
of air. Vol.II p.
29 et seq.

- (29) IBID.
- (30) LAVOISIER Traité Élémentaire
de Chimie .
- (31) IBID. P. 38.
- (32) PRIESTLEY Op. cit. p. 226 et
seq.
- (33) LOWRY Inorganic
Chemistry P. 77 et
seq.
- (34) BLACK Experiments upon
magnesia alba,
quick lime and
other alkaline sub-
stances.
Alembic Club
Reprints No. 1.
- (35) BLACK Elements of
Chemistry.
- (36) LAVOISIER Opuscules
physiques et
Chymiques.
- (37) SLARE Phil. Trans.
Vol. XVII P. 898
1693.
- (38) PRIESTLEY Op. cit. Vol. III.
- (39) LAVOISIER Memoires de l'
Académie des
Sciences 1777 P.185.
- (40) LAVOISIER Oeuvres P. 182.
- (41) PRIESTLEY Phil. Trans. 1772
Vol. 62. P. 188.
- (42) BOYLE Phil. Trans. 1670
Vol. 5 P.2043.

- (43) IBID P. 2011.
- (44) BOERHAAVE Institutione Medicae
1727 P. 279 De
Respiratione.
- (45) LE CAT Traité de l'existence
de la nature et des
propriétés du Fluide
des Nerfs 1745.
- (46) DRAKE Phil. Trans. 1702
Vol. 23 P. 1230.
- (47) IBID. P. 1228.
- (48) VAN SWIETEN Comment in Boerhaave,
Aphor. P. 271.
- (49) HOUSTON Phil. Trans. Vol. 39
P. 230 1728 Experimenta
de Perforatione Thorac-
is eiusque in
respiratione effectibus.
- (50) HALES Haemastatics P. 77
1732.
- (51) BERTIER Physique des corps
animés 1755.
- (52) DE BREMOND Memoires de l'Académie
des Sciences. 1739 P.333
- (53) MARTINE Medical Essays Vol. 1
Art. 12.
- (54) WHYTT Essay on the Vital and
other Involuntary
Motions of animals.
1751. Section VIII.
- (55) IBID P. 176.
- (56) HARTLEY Observations in Man,
His Frame, his Duty
and his Expectations.
1749.

- (57) HALLER Elementa Physiologiae
Corporis Humani.
Vol. III.
- (58) HALLER Op. cit. P. 238.
- (59) HALLER Op. cit P. 232.
- (60) HALLER Lectures on
Physiology P. 241
Lecture X.
- (61) HALLER Op. cit. P. 231.
- (62) MAYOW Op. cit. P. 283.
- (63) HAMBERGER De Respirationis
Mechanismo et usu
genuino dissertatio.
1748.
- (64) HALLER De Respiratione Experi-
menta anatomica. 1747.
- (65) HALLER Memoires sur la nature
sensible et irritable
des parties du corps
animal.
Expériences de Mr.
Zinn. Exp. IX.
- (66) HALLER Memoires sur la nature
sensible and irritable
des parties du corps
animal.
Memoire II. Exp. 210-225
- (67) WINSLOW Memoires de l'Academie
Royale des sciences.
1738. P.65.
- (68) SENAC Memoires de l'Academie
Royale des Sciences
1729 P. 118.
- (69) SENAC Op. cit. 1724 P. 159.

- (70) GIBSON Farrier's Guide.
1720 P. 73.
- (71) WINSLOW Exposition anatomique de la structure du corps Humain.
Tome II. P. 394.
- (72) HOADLY Three Lectures on the Organs of Respiration. 1740.
- (73) MAGENDIE Précis Elémentaire de Physiologie
Tome II. 1817.
- (74) BELL Phil. Trans. 1821
P. 405.
- (75) IBID. 1822. P. 296
- (76) IBID. , 1822 P. 298.
- (77) LE GALLOIS Expériences sur le principe de la vie
1812 P. 36.
- (78) LORRY Académie des Memoires des sarrants etrangers.
Tome III. P.366.
- (79) LE GALLOIS Op. cit. P. 44.
- (80) LE GALLOIS Op. cit. P.335
et seq.
- (81) FLOURENS Recherches Experimentales sur les propriétés et les fonctions du Systeme Nerveux dans les animaux vertebres
1842. P.172 et seq.
- (82) FLOURENS Op. cit P. 199.

- (83) MARSHALL HALL Lectures on the
Nervous System, 1836
P. 25.
- (84) GIERKE Archiv. F. die
gesammte Physiologie.
7. 583. 1873.
- (85) MARTIN & BOOKER J. of Physiol. 1. 370.
1878.
- (86) MISLAWSKY Centralblatt f. die
med. Wissenschaften.
27. 1885.
- (87) GAD Archiv. f. Physiologie
1893 P. 75.
- (88) LEWANDOWSKY Arch. f. Anat. u.
Phys. P. 195. 1896.
- (89) BROWN Proc. of the Physiol.
Soc. May 16, 1914.
- (90) TREVAN Proc. of the Physiol.
Soc. July 15 1916.
- (91) BARCROFT Proc. of the Physiol.
Soc. July 12, 1919.
- (92) LUMSDEN J. of Physiol. 57 P.
153. 1923.
- (93) IBID. P. 354.
- (94) LUMSDEN J. of Physiol. 58.
P. 81.
- (95) HUGGETT & MELLANBY J. of Physiol. 39.
P. 392.
- (96) LUMSDEN J. of Physiol. 58.
P. 124.
- (97) ZUNTZ Archiv. f. Physiologie
1897. P. 397.

- (98) FRIEDLÄNDER & HERTER ... Zeit. f.
Physiol. Chemie.
2, 99 & 3, 19.
- (99) BETHE Erget. d. Physiol.
V. p. 250. 1906.
- (100) ZUNTZ & LOEWY Höhenklinik und
Bergwanderungen
1906.
- (101) HILL & FLACK J. of Physiol. 37.
P. 73.
- (102) WINTERSTEIN Pflügers Archiv.
138. 167 1911.
- (103) WINTERSTEIN Zentrib. f.
Physiol. 24. P.811
1910.
- (104) HALDANE & LORRAIN SMITH.. Journal of Pathology
and Bacteriology.
Vol. I. P. 168.
1892.
- (105) SCOTT J. of Physiol. 37.
301. 1908.
- (106) HALDANE & PRIESTLEY J. of Physiol. 32.
P. 225. 1904.
- (107) HALDANE & POULTON J. of Physiol. 37
P. 390. 1908.
- (108) DOUGLAS & HALDANE J. of Physio. 38. P.
420.
- (109) HERING & BREUER Wien sitzemgsb.
Abt. II. P. 672 1868
- (110) HERMAN'S PHYSIOLOGY p. 167.
- (111) LEWANDOWSKY Ueber Schwank ungen
des Vagus stromes
bei Volumänd -
erungen der Lunge -
Pflügers Arch. f.d.
ges. Physiol. Bd.
LXXIII. S. 288. 1898

- (112) ALCOCK & SEEMAN Proc. of the Physiol.
Soc. 1904 XXX.
- (113) ALCOCK & SEEMAN Pflügers Arch f.d.
ges. Physiol.
Bd. CVIII, S. 426
1905.
- (114) EINTHOVEN Q. J. of Exp.
Physiol. 1908. 1,
243.
- (115) WINTERSTEIN Pflügers Archiv.
138, 159, 1911.
- (116) BORUTTAU Nagel's Handbuch der
Physiologie I. P. 46.
- (117) LOEWY Archiv. f. die
gesamte Physiol.
42 273.
- (118) MARKWALD Zeit f. Biol. XXIII.
P. 149 1887.
- (119) LEWANDOWSKY Arch. f. Anat. u.
Phys. Phys.
Abth. P. 195 & 483.
1896.
- (120) KNOLL Beiträge zur Lehre v.
d. A^thmungsinⁿervation
- Mitth. I. Sitzb.
d.k. Akad. d.
Wissensch. Bd. LXXXV
Abth. iii.
- (121) GAD Die Regulirung d.
Normalen Athmung.
- (122) HEAD J. of Physiol. 10 1.
- (123) AUER & MELTZER Proc. of the Amer.
Physiol. Soc. 1911-
1912. XXIX.
- (124) IBID. XXXII.

- (125) BARRY J. of Physiol. 45.
P. 473. 1912.
- (126) MARTIN & HARTWELLJ. of Physiol. 2 P.24,
1879.
- (127) HOUGH Studies from the Biol.
Lab. John Hopkins
University 5, 91, 1893.
- (128) SCHAFER & MACDONALD . Proc. of the Physiol.
Soc. May 30 1925.
- (129) SEWALL & POLLARD J. of Physiol. 11 101.
1890.
- (130) ORR & WATSON J. of Physiol. 46.337.
- (131) MIESCHER Arch. f. Anat. u.
Phys. 1885, P. 335.
-