§1. The Classical Contribution.

In the Ebers and Hearst papyri, poor fragments of old Egyptian medical lore, and in the equally scanty vestiges of Babylonian and Jewish medicine, we neither expect nor find much knowledge of the functions of the lung. It is to Greece, home of the arts and birthplace of science, that we naturally turn for the beginnings of the physiology of the lung. Yet we must not expect too much from the Greeks: investigation of the functions of an organ demands previous familiarity with its structure,—and the Greeks had no microscope; study of the \( \text{O}_2-\text{CO}_2 \) exchange involves a knowledge of the chemistry of these gases,—and the Greeks knew no chemistry; an adequate theory of respiration presupposes a correct idea of the circulation of the blood,—and the Greeks had an erroneous idea. It is not surprising, then, that their contribution to our knowledge of the functions of the lung is very slender.

In the early period, before the Grecian civilisation had reached maturity, we find views so palpably absurd
that they are scarcely worth mentioning. Empedocles of Sicily, for example, in the 5th century B.C., taught that air-containing ducts (πόροι) traversed the body in every direction.

The golden age of Greece — the age of Plato and Socrates in philosophy, of Sophocles and Euripides in drama, of Hippocrates in medicine — witnesses the real beginnings of anatomical and physiological research, and ensures that future views, if not necessarily accurate, will at least not be ridiculous. Hippocrates himself, though he dwells repeatedly on the pathological significance of various types of respiration, seems to have ignored the purpose and mechanism of breathing; but one of his immediate successors, Erasistratus of Alexandria, suggested that air or “pneuma” passed from the air-passages to the arteries and was carried by the latter through the body. A vague theory, no doubt, but the first gleam of light amid the darkness!

After the collapse of Alexander’s empire Physiology and the other sciences “left their Parnassus for the

* See in particular Vol. 2 of Littre’s edition.
Latian plains."

Over the work of the Pneumatists — who maintained that air, drawn from the lungs to the left side of the heart, was in that organ divided into "Psychic Pneuma" and "Natural Pneuma" — over the achievements of such Roman Greeks as Asclepiades and Rufus (who accepted the theory that arteries carry only air), and such true-born Romans as Celsus, we must pass in silence to reach the greatest mind of ancient — if not of all — medicine.

Galen's ideas on the respiratory and circulatory systems may be summed up as follows: — In diastole the heart dilates and draws in blood (manufactured from food in the liver) to the right side from the Inferior Vena Cava, and air (taken in by the lungs) to the left side from the "Vein-like Artery," i.e. the Pulmonary Vein. From the right ventricle some of the blood passes through invisible pores. *Galen usually speaks of the pores as invisible, although in "Natural Faculties" III & IV he talks as if he had actually seen the perforations. Possibly he saw recesses between the columnae carneae and mistook them for perforations.
in the septum into the left ventricle, and there air and blood combine, under the influence of the innate heat of the heart, to form the vital spirit.

In systole the heart collapses and drives the crude blood from the right ventricle into the veins, including the pulmonary artery; while from the collapsing left ventricle the vital spirit passes into the arteries, including the pulmonary vein. Part of this vital spirit is carried to the tissues and provides nourishment for them; another portion reaches the brain and is there transformed into the pure "psychic pneuma" which, transported by the nerves, renders possible all the higher functions of the body; and that part of the vital spirit which is taken to the lung carries with it certain "fuliginous vapours" which are duly excreted in expiration.

It is obvious, then, that although Galen has not grasped the pulmonary circulation he realises that blood and air travel from the heart to the tissues. Although his erroneous ideas on "vital spirit" and the permeability of the septum hindered physiological research for many
centuries, we must not forget that Galen was the first to suggest that air played a part in the nourishment of the tissues, and that he gave the first valid explanation of the mechanism of respiration.

With the death of "the first and only experimental physiologist before Harvey" in the year 201 A.D., the classical contribution to our knowledge of respiration comes to an abrupt close.

§ 2. The Italian Contribution, 1500-1700.

It seems a far cry from the Rome of Galen to "Fair Padua, nursery of arts" (Shakespeare) in the 16th century, yet in 1500 man's knowledge of the functions of the lungs was no greater than it had been in 200. The Byzantine physicians — e.g. Oribasius and Aeginata — had been torch-bearers of knowledge rather than original workers; the Arabs — including even Avicenna — had merely collected and transmitted the learning of the past; and
the scientists of medieval Christendom—despite a few brave thinkers like de Mandeville (the surgeon who dared to say, "God did not exhaust all His creative power in making Galen")—declined experiment and induction, in favour of servile adherence to the doctrines of antiquity.

For thirteen centuries the dark night of authority lasted, then, in the middle of the 16th century, came the redawn of the day of reason. The morning star that heralded this new day was a young Belgian, Andreas Vesalius, who, already occupying a professorial chair at Padua, dared at the age of 27 to question the omniscience of Galen. Vesalius himself added nothing to the knowledge of the physiology of the lung, but by substituting nature and observation for books and authority he rendered possible the work of later physiologists.

In 1553, exactly ten years after the publication of Vesalius' "Fabrica Humani Corporis," Servetus printed his "Restitutio Christianismi." In this work the theological physician, who a few months later was burned at
the stake for "the crime of honest thought", described the pulmonary circulation, rejected the now unnecessary idea of pores in the septum, and stressed that "the ruddy colour is given to the vital [i.e. arterial] blood by the lungs, not by the heart."

In the first section of this sketch of the development of our knowledge of the functions of the lungs it was pointed out that before these functions could be understood three lines of investigation had to be followed—circulatory, histological, and chemical. With the description in the "Reditus Christianismi" of the pulmonary circulation a gigantic advance had been made along the first of these three lines.

* "The subtle blood is driven from the right ventricle by a long passage through the lungs. It is worked on by the lungs & made ruddy, & from the pulmonary artery is poured into the pulmonary vein. Then in the pulmonary vein it is mixed with the inspired air & freed from sooty matter by expiration. So at length the complete mixture is drawn by the left ventricle through the Diastole, still fit to become the vital spirit."— Reditus Christianismi, 1553, p.171.
Eighteen years later Andrea Cesalpino ("Quaestiones Peripateticae," 1571) described the systemic circulation, without, however, giving adequate proof of his statements; and a generation after Cesalpino's work had been forgotten an English physician who had studied at Padua, William Harvey, rediscovered the circulation and supported his discovery by logical arguments and convincing experiments. With Harvey the first line of preliminary investigation is nearly complete: chemical and histological ignorance alone bars the way to a complete understanding of the functions of the lungs.

Before Harvey's death the microscopic structure of the lung was also investigated. Malpighi, the real founder of the science of histology, published in 1661 his "De Pulmonibus Observationes Anatomicae." "Up to that time"—says Foster*—"little or nothing was known of the real structure of the lung. It was spoken of as fleshy, and its substance, which Fabricius had compared to tow, was held to be a porous parenchyma.

* Sir Michael Foster, "Lectures on the history of physiology," lect. 4.
in which the minute divisions of the blood-vessels on the one hand and of the windpipe on the other were lost."

Malpighi, using the compound microscope, which had been invented about 70 years before, described the vesicular nature of the lung, showed how the divisions of the bronchi end in the dilated air vesicles, demonstrated the network of capillaries winding over these vesicles, and indicated that the capillaries joined the minute arteries to the minute veins. Although later histologists—e.g. van Leeuwenhoek in Holland some seven years afterwards—amplified Malpighi's reports, we may say that for all practical purposes the anatomical basis for the true conception of respiration was furnished by the Italian's work.

In sketching the circulatory discoveries and histological studies of the 16th and 17th centuries we have of necessity ignored men who pursued other lines of investigation. Before we pass on, however, four of these must be mentioned. Fabricius, Harvey's teacher at Padua, wrote a treatise, "De Respiratione et eius Instrumentis,"* in which he attempted to deal with the general mechanism of respiration and suggested that the whole purpose

* Written in 1599, published in 1603.
Of the lung is to provide air for the "vein-like artery"; Malpighi's friend, Borelli, in his "De Motu Animalium" (1680) investigated inter alia the mechanics of respiration, and—even though his ultimate theory of muscular action was incorrect—he at least swept away many current superstitions about the functions of the lung; the Belgian mystic, van Helmont, who invented the word "gas" and was the first person to describe Carbon Dioxide ("gas sylvestre"), may be said to have founded modern chemistry; and Silvius de Leyden realised that in some manner inspired air alters the blood, and—although his statements are vague and his explanation is wrong—he at least showed that this alteration of the blood was a problem to be investigated.

§ 3. English Investigators of the 17th Century.

Sir George Newman says, "The revival of medicine passed in the direct line from Padua to Leyden, from Leyden to Edinburgh."* However true this may be of medical progress in

general, in the particular branch which we are considering the first great non-Italian centre of enlightenment is neither Leyden nor Edinburgh, but London. In spite of a few Italians like Borelli and Malpighi and a few Dutchmen like Silvius and van Leeuwenhoek, the investigation of the physiology of the lungs remains almost entirely in the hands of Englishmen—mostly Londoners—for a century after Harvey’s discovery.

The principal contribution of the English scientists of this period towards our knowledge of the functions of the lungs is some conception of the nature of the inspired and expired gases. The first steps in what Sir Clifford Allbutt has called “the pathetic quest for oxygen” were taken by Boyle and Hooke just before Harvey’s death. In 1660 Robert Boyle showed that in a vacuum candles were extinguished and mice died,—thus proving that air, not merely movement of the chest, was essential to the due effect of breathing, and that the change which was effected in breathing was identical with that which occurred in the burning of a candle. Seven

* R. Boyle, “Nova experimenta physico-mechanica de vi aëris elastica”, Rotterdam, 1669.
years later Robert Hooke, by showing than an animal could be kept alive by artificial respiration without movement of the lungs, verified that air was the essential factor and movement of the lung a mere incidental.* Moreover, although he did not apply it to respiration, Hooke suggested that flame might be due to the action of a part of the air,—i.e. he realised that air was not necessarily a single, indivisible substance.

In 1669 Richard Lower published his "Tractatus de Corde," in which—in addition to giving a very accurate description of the anatomy of the heart—he proved that the colour change from dark venous to bright arterial blood occurred in the lung, not in the heart as had previously been supposed. "And he at once took the next step and drew the further conclusion that the change in colour was due not to mere exposure alone but to the blood taking up some of

*R. Hooke, "A supply of fresh air necessary for life," Phil. Trans., 1664, vol. 2, p. 539 et seq. To prove that Hooke fully understood the implication of his experiments we quote his own words: "...It was not the subsiding or movelessness of the lungs that was the immediate cause of death, or the stoppage of the circulation of the blood through the lungs, but the want of a sufficient supply of fresh air."
the air." *

Pepys could write of respiration; "It is not to this day known or concluded among physicians, nor to be done either, how the action is managed by nature or for what use it is." Yet even while Pepys was writing a young man of 25 came very near to solving the whole problem.

John Mayow (1643-1679) published five tracts, two of which — "De Respiratione" and "De Sol-Nitro et Spiritu Nitro-Aereo" — are highly important documents in the history of the investigation of the phenomena of respiration. In these tracts, which in their conciseness and clarity are reminiscent of Harvey's work, Mayow records convincing experiments and draws precise, logical conclusions.

His two main deductions may be given in his own words:— (1) "Nempe imprimit pro concesso habeo, Alenum particularis quaedam, quas alibi Nitro-aeras noncupavimus, ad Ignem confundam omexeco necessarias continere; atque

* Foster, Lectures on the History of Physiology, - lect. 7.
* Pepys' Diary, Bright's edition, 1900. - v, 191.
caer her flammeae deflagrationem ab aere exhauini, et absuni; ita ut idem particulus istis deprivatus, in futurum et ignem sustinendum prorsus invidens evadat, ut supra ostendum est."—Tractatus Quinque, p.96. ["In the first place, then, I take it for granted that the air contains certain particles termed by us elsewhere Nitro-aereal, which are absolutely indispensable for the production of fire, and that these in the burning of flame are drawn from the air and removed, so that the latter when deprived of these particles ceases to be fit for supporting fire, as has been shown above."]

(2) "Utique credendum est, Animalia, Ignemque particulas e iisdem generis ex aere exhaurine."—p.107. ["Indeed we must believe that animals and fire draw particles of the same kind from the air."]

If the modern word "oxygen" were substituted for the phrase "nitro-aereal particles" Mayow's statements might pass for extracts from a 20th century textbook.

Mayow understood that part of the air was "active". He realised, unlike Stahl a generation later, that this active portion entered into combination with the substance burned. And he recognised that the function of respiration is simply to cause
an exchange of gases between air and blood,—the latter taking up the "nitro-aereal particles" and setting free vapours engendered in the body.

Unfortunately, Mayow made one mistake: he tried to identify his nitro-aereal particles with the elastic force of the air. And by the irony of fate, it came about that, while Mayow's chemical theories fell on barren soil, his erroneous ideas on elastic force flourished for nearly a century.

From our present point of view the most important of Mayow's tracts is the "De Respiratione" (1668), a short treatise in which the fruits of much careful investigation and brilliant thought have been condensed into about 8000 words. In this treatise Mayow describes the mechanics of breathing with an accuracy that is far in advance of all earlier treatises on the subject. He shows that in inspiration the chest is enlarged by the raising of the ribs (by the intercostal muscles) and the descent of the diaphragm (through its own contraction). Air, he explains, enters the lungs simply because the atmospheric pressure drives the air in to fill the increased space afforded by the
enlarged and dilated thorax. In expiration, air is expelled as a result of the passive relaxation of the intercostals and diaphragm.

As for the purpose of breathing,—Mayow rejects the view that the primary purpose is to cool the blood, but points out that the pulmonary circulation is too elaborate constructed to be simply a means of transit of the blood from the right to the left side of the heart. He agrees with Boyle and Hooke that the function of respiration cannot be simply to move the blood or break it into particles; and finally he concludes that something must pass from the air to the blood: “On the one hand it clearly appears that animals exhaust the air of certain vital particles which are of an elastic nature. On the other hand there cannot be the slightest doubt but that some constituent of the air absolutely necessary to life enters into the blood in the act of breathing.”

Mayow even gets a glimpse of the part played by oxygen in the tissues. Near the end of the De Respiratione he suggests* that probably the nitro-aereal particles are necessary for

* P. 208 of the Alembic Club Reprint.
all muscular movements, and that "in exercises and violent movements there is need of more intense and more frequent respiration, not so much that a greater flow of blood may pass freely through the lungs... but because there is a great expenditure of nitro-aereal salt in consequence of the various effervescences made in the contraction of the muscles."*

On the subject of expiration Mayow again comes very near the truth. He says, * "Along with the air driven out from the lungs, the fumes which are raised by the fermentation of the blood are also blown out."+

It is difficult to over-estimate the significance of Mayow's discoveries. The De Respiratione makes all the earlier accounts of the physiology of the lungs appear childish. Yet this work of genius—a work which one of the greatest of modern physiologists has termed "an exposition which might almost find its place in a text-book of the present day"—was produced by a man only 25 years of age.

* P. 209 of the Alembic Club Reprint.
+ P. 205 of the Alembic Club Reprint.
† Foster, lectures on the History of Physiology,—lecture 7.
One might imagine that after the publication of Mayow's tracts the fundamental facts about the function of the lungs would have been known to the civilised world. Actually, like the discoveries of Mendel in another field and in a later century, Mayow's work on respiration and on the chemistry of the air was unrecognised and unbelievable. Professor Gotch has suggested that the disregard of Mayow's views was largely due to a garbled English extract of his Latin text, which some literary hack made for the Royal Society.

At any rate, in spite of the brilliant work of Harvey, Boyle, Hooke, Lower, and Mayow, at the close of the 17th century "the immense ocean of truth"—to adapt Sir Isaac Newton's words—"still extended itself unexplored."

§4. The Investigators of the 18th and 19th Centuries.

The earlier half of the 18th century is a somewhat

* Gotch, Two Oxford Physiologists, 1908, pp.35-38.
barren period. The only investigators whom we need mention are Stahl, Boerhaave, and Hales.

Georg Ernst Stahl (1660-1734) played an unfortunate part in the history of the investigation of respiration. By originating the phlogiston theory—that when a body burns it gives off a hypothetical substance, phlogiston—he undid the work of Mayow and greatly impeded the discovery of oxygen; by asserting that the purpose of the movements of the thorax and lungs was to regulate the passage of blood through the pulmonary blood vessels he re-established an already disproved theory of respiration; and he obscured the vital truth of the suggestion that something passes from the air to the blood by remarking: “However these things may be, these considerations, interesting perhaps to the curious, add absolutely nothing to medical practice; and it is not meet to waste any more time upon them.”

Hermann Boerhaave (1668-1738) adopted a more cautious attitude. In his Elements of Chemistry the Leyden professor declares that since all living things require air, air must contain the secret food of life. But he can only
add,—"But what it really is, how it acts, and what exactly it brings about is still obscure."

Thirdly, Stephen Hales (1677-1741) added nothing directly to our knowledge of respiration. His writings, however, "contain the first clear enunciation of the existence of gases in a free and in a combined state," and by this enunciation they greatly facilitate future researches.

The second half of the 18th century compensates fully for the bleakness of the first half. Haller, Hamberger, Spallanzani, Black, Priestley, Lavoisier,—directly or indirectly all these contributed to the elucidation of the problems of respiration.

Let us take Haller first. The greatest physiologist of his time, and perhaps the only man since Aristotle to achieve eminence in five different subjects—physiology, anatomy, botany, poetry, and fiction—Albrecht von Haller (1708-1778) devoted the third volume

of his "Elementa Physiologicae" to respiration. Fully aware that this subject—like other branches of physiology—had suffered from theoretical conclusions unsubstantiated by experiment or observation, Haller avoided speculation and theory as far as possible and devoted the greater part of his time to the accurate ascertainment of facts. He was particularly successful in his work on the mechanism of breathing. The essentials had, of course, been known previously, but Haller was the first to investigate in detail the actions of the various muscles concerned in respiration.

Haller tried to be an experimental physiologist but, living as he did in an age of theories and systems, he could not manage to keep entirely to the narrow path of logic and proved fact. One of the occasions on which he strayed was when he described the use of breathing: air, he suggested, lost its "elastic nature" in the lungs, entered the blood, and acted as a cement, holding together the "earthy elements."

Dr. Singer places Haller along with Stahl and Boerhaave

*Singer, A Short History of Medicine, 1928, p. 151.
in the group of "theorists", but Haller's patient and thorough investigation of the mechanical side of respiration is more than mere theory. It is a worthy enquiry into a previously neglected subject.

The exploration of this subject was continued during Haller's lifetime by Hamburger, and then—after a gap of over a century—by Martini and Hartwell.

While Haller was explaining how breathing occurs, the gases concerned in respiration were at last being discovered,—or,—in some cases, re-discovered. Joseph Black (1728-99), the great Scottish chemist, sounded the death-knell of the phlogiston theory by his discovery, in 1754, of Carbon Dioxide,—the "gas sylvestre" that van Helmont had already detected 130 years before. Black termed his new gas "fixed air", and seems at first to have identified it with the inrespirable portion of the atmosphere. He corrected this error, however, as soon as Rutherford had recognised the gas which Chaptal later named "Nitrogen".

As Black rediscovered van Helmont's "gas sylvestre", so Priestley, Scheele, and Lavoisier re-discovered
Mayow's "nitro-aereal salt". Priestley and Scheele isolated oxygen before Lavoisier did, but they were too obsessed with the phlogiston theory to realise the tremendous importance of their discovery. Priestley, for example, tried to explain respiration as follows: - Ordinary air contains a certain amount of phlogiston but can absorb more until the saturation point is reached. In breathing (or in combustion) phlogiston is given out; and accordingly, this process can take place in ordinary air but becomes impossible as soon as the air is saturated with phlogiston. Dephlogisticated air (i.e. oxygen) supports breathing and combustion better than does ordinary air, because it is at first free from phlogiston and can therefore absorb more of this substance. As for Black's "fixed air", it is normally combined with ordinary air but is split off when the air becomes saturated with phlogiston.*

Priestley, then, tried to fit new facts to an old theory. It was left for Lavoisier to interpret the significance of the

discovery of oxygen. But before we turn to the Frenchman we must mention another English scientist.

Henry Cavendish (1731-1810) has been termed "perhaps the most notable man in the 18th century, ... who did as much as any man of that century, except Dalton, to put medicine upon a scientific basis." He contributed, indirectly at least, to the investigation of respiration by the discovery of hydrogen, of the composition of the atmosphere, and of the composition of water.

In his paper On the nature of the principle which combines with metals during their calcination (1775) Antoine Laurent Lavoisier (1743-1794) gives, more or less, the same facts as Priestley, but without any veil of preconceived ideas. As Dr. Singer puts it, "If clear grasp of the implication of discovery be made the test, Lavoisier must be regarded as the discoverer of oxygen."

In 1775, then, Lavoisier proved conclusively that when metals were burned in air, the air

* Gorton, The History of Medicine, 1910. - Vol. 1, p. 381.
* Singer, A Short History of Medicine, 1928. - p. 152.
lost some constituent which the metal gained. This constituent he later named "oxygine principle."

From combustion Lavoisier turned to respiration. In his Experiments on the respiration of animals and on the changes which the air undergoes in passing through the lungs (1777) he points out (a) that in respiration, as in combustion, air loses oxygen; and (b) that expired air—unlike air in which a metal has been oxidized—contains carbon dioxide. He concludes that there are two possible explanations:- "Either the portion of the air eminently respirable contained in the air of the atmosphere is converted into aeriform calcic acid,* or a change is effected in the lung by which on the one hand the air eminently respirable is absorbed, and on the other hand the lung substitutes in its place in nearly equal volume a portion of aeriform calcic acid." He discusses these possibilities and suggests that the second

* Lavoisier's name for CO₂.
is the more likely, in which case the red colour of arterial blood might be due to a combination with the "eminently respirable air."

When Lavoisier published these conclusions his researches into respiration were by no means at an end. Three years later he and Laplace showed that the amount of heat given out by an animal during any period is approximately the same as that given out by the oxidation of enough carbon to produce a volume of carbon dioxide equal to that produced by the animal. *From this they deduced that respiration is essentially a form of slow combustion of carbon.

Five years later Lavoisier had to modify this view slightly. In 1785 he discovered that not all the inspired oxygen reappears as carbon dioxide. Using Cavendish's discovery of the composition of water he argued that the oxygen which does not reappear must either unite with the blood, or—more probably—combine in the lungs with hydrogen to form

Finally, near the end of his career, Lavoisier made a false step. In their memoir on The Transpiration of Animals (1790) Lavoisier and Seguin explain how the carbon and hydrogen from food are oxidized and how carbon dioxide and water are excreted by the lungs; but they declare that a hydrocarbonous fluid transudes into the bronchi and that it is in the lungs and bronchi that the oxidation takes place.

In spite of this last error Lavoisier's contribution to our knowledge of the functions of the lungs is far greater than that of any of his contemporaries. As Sir Michael Foster says, "He brought our knowledge of respiration very nearly to its present condition."*

The idea of a hydrocarbonous fluid transuding into the bronchi was immediately disputed. Lagrange and his assistant, Hassenfratz, denied that the oxidation of carbon and hydrogen occurred in the

* Foster, Lect. on Hist. of Physiol.,-lecture 9.
lungs or bronchi. They maintained that the process took place in the blood. Although they were nearer to the truth than were Lavoisier and Seguin, the view of the latter continued to hold the field.

While the controversy was still continuing, the Abbé Lazaro Spallanzani (1729-1799) investigated the respiratory exchanges in cold-blooded and warm-blooded animals, and made at least two important observations: (1) that cold-blooded animals can live for a time in an atmosphere of hydrogen and continue to give off carbon dioxide; and (2) that the excised tissues of a freshly killed animal can consume oxygen and produce carbon dioxide. Spallanzani’s results should have helped to destroy the theory of Lavoisier and Seguin, but neither his carefully conducted experiments nor the well-reasoned arguments of W. F. Edwards‡ a generation later convinced the scientific public.

‡ Edwards, The Influence of Physical Agents upon Life, 1823.
that there was any reason for doubting the established view.

However, in 1837 Gustave Magnus*, using a Sprengel's air-pump, proved definitely that both venous and arterial blood contained both oxygen and carbon dioxide, though in different proportions. This gave the death-blow to the theory that carbon and hydrogen were oxidised in the lungs or bronchi.

With the acceptance of Magnus's conclusions the bulk of the fundamental facts about the physiology of the lungs may be regarded as known: the preliminary work on the pulmonary circulation, the histological structure of the lung, and the chemistry of the gases concerned in respiration, had been completed; and it was recognised that the main functions of the lungs were to transfer oxygen in some unknown manner from the inspired air to the arterial blood and to transfer carbon dioxide in some equally unknown manner from the venous blood to the

alveolar air. These facts were known, thanks to the investigations of Borelli, Boyle, Hooke, Lower, Mayow, Black, Cavendish, Priestley, Lavoisier, and Magnus;—or (as Garrison puts it) to “the work of three mathematicians, two physicists, and five chemists.” *

Many of the finer points had yet to be investigated, but—curiously enough, in view of the fact that the latter half of the 19th century is one of the greatest periods of physiological research—most of them were not investigated until after the end of the century. We shall therefore simply mention, without going into details, a few of the more important discoveries of the 19th century, and then pass at once to the researches of the present century.

In 1829 and subsequent years Thomas Graham † of Glasgow discovered the laws governing the diffusion of gases. The recognition of these laws rendered possible an investigation of the means by which oxygen passed

* Garrison, Introd. to Hist. of Medicine, 1913, p. 259.
to, and carbon dioxide from, the capillaries. This line of enquiry was taken up by Durocher at once and by Graham himself two decades later, but the full elucidation was left to Hamburger and other workers of the 20th century.

Legallois in 1830 made the first attempt to localise the respiratory centre in the medulla, and Flourens* and various others followed his lead. This investigation, however, hardly comes within the scope of an essay on the functions of the lungs.

Weber's discovery, in 1845, of the inhibitory action of the vagus nerve led to a great deal of work on the nervous control of the lungs. From our present point of view the most important part of this investigation is the discovery of Hering and Breuer, in 1868, that one of the functions of the lungs is to control themselves — since the distension and contraction of the lungs

lungs are in themselves the normal stimulus of the vagus.

The mechanics of respiration had been studied in considerable detail by Haller and Hamburger in the middle of the 18th century. After a gap of 120 years H. N. Martin and E. M. Hartwell re-opened this subject in 1879, and confirmed and amplified the conclusions of the earlier workers.

Another discovery, even though it does not relate directly to the functions of the lungs, should perhaps be mentioned here. Eduard F. W. Pflüger* (1829-1910) showed in 1868 that the essential changes of respiration, which according to Lavoisier occurred in the lungs and according to Magnus occurred in the blood vessels, really took place in the tissues. It is to be noted, however, that while Pflüger showed that these changes occurred in various tissues he did not ascertain to what extent, if any, they occurred in the lungs themselves.

To mention all the significant discoveries of

* Archiv für der gesamte Physiologie, Bonn, 1868, i, 61-106.
the later 19th century — those of Regnault and Reisset, Chapman and Brüecker, Poiseille, Grieske, Rosenthal, Hoppe-Seyler, Marzet, Pettenkofer and Voit, Spech, Saint Martin (to name only a few of the investigators) — would swell this essay to the size of a textbook. We shall therefore omit these lesser, but not altogether unimportant, discoveries, and pass to the 20th century.

§ 5. Recent Developments: 1900-1935.

The truth of Rowland's dictum, "All the sciences are linked together and must advance in concert," becomes increasingly obvious as we reach modern times. Again and again we find that discoveries which at first sight appear to have no connection with the lung have indirectly thrown new light on the functions of that organ. Thus the work of Rohde (1910) and of Barcroft and Piper (1912) on the oxygen consumption of the tissues seems to have no relation to the physiology
of the lung. Yet it was by adopting the methods and using the results of these workers that Evans in 1912 showed that the metabolism of lung tissue amounts only to 0.015 cc. per gramme per minute; and it was this discovery which finally disposed of the theory that a considerable amount of oxidation occurs in the lungs.

If, however, we neglect incidental information acquired through experiments which do not relate directly to the lung, we find that most of the recent investigations of the physiology of that organ fall into one or two groups,—a group concerned with how the oxygen passes from the alveoli to the capillaries, and a group concerned with the regulation of respiration.

The question of the passage of oxygen from the lungs to the blood raises the age-old "vitalistic" and "mechanistic" argument. On the one hand, the pulmonary exchange may be regulated by the laws of

* The metabolism of lung tissue is about ⅓ of that of liver, and less than ⅓ of that of heart or suprarenal.
diffusion alone: if this be true, then, since a gas always diffuses from a place of higher tension to one of lower tension, the oxygen tension of the arterial blood can never rise above that of the alveolar air and the carbon dioxide tension can never fall below it. On the other hand it is possible that the pulmonary exchange is not a mere diffusion but a vital process: if this be true, then the arterial oxygen tension could conceivably rise above the oxygen tension of the alveolar air.

Christian Bohr, in his “Blutgase und respiratorische Gaswechsel” (1909), supported the vitalistic theory—maintaining that the alveolar epithelium can actively secrete oxygen in the direction of the blood. This view was immediately challenged by Krogh.* Krogh’s experiments in 1910 demonstrated that the oxygen tension in the arteries was less than that in the alveoli, and that the carbon dioxide tension was equal to, or greater than, that of the alveolar air; and in support of his

"mechanistic" theory Krogh pointed out that the flattened, "pavement" epithelium of the lung is totally unlike the varieties of epithelium which are known to secrete.

Haldane and Douglas*, however, accepted Bohr's view with modifications: they stated that normally pulmonary epithelium does not secrete oxygen, but that in a high altitude it can develop the power of doing so.

Bayliss and others pointed out that it was highly unlikely that a secretory function should have been evolved to meet such a rare need; and Starling showed that, whereas in secreting glands the mechanism works in one direction, here it works in both; for when a person breathes fife damp he at once loses oxygen from his blood. These points do not, of course, explain the results obtained by Haldane and Douglas when working at high altitudes; but in 1920 a group of investigators led by Barcroft carried out

* (1) Douglas & Haldane:—Journ. Physiol., 1912, 44, p. 305 et seq.;

experiments similar to those of Haldane and Douglas, using, however, an air-tight chamber with diminished oxygen tension instead of a high altitude, and obtained diametrically opposite results: they found that both in rest and in muscular exercise the arterial blood showed a lower oxygen tension than the alveolar air. Two years later a different group of investigators, again led by Barcroft, measured the oxygen pressures of alveolar air and arterial blood at an altitude of 14,200 feet, and found that the oxygen tension of the blood did not rise above that of the alveolar air.

At the moment the bulk of the evidence appears to be against the possession by the lung of any secretory function. In one of the standard text-books of physiology, Professor Evans goes so far as to say, “The view that, in the interchange of gases in the lungs, the membrane between the blood and the alveolar air plays simply a passive part is now almost universally accepted.” Yet we cannot absolutely

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* Barcroft, Binger, Bock, Doggart, Forbes, Harrop, Meakins, and Redfield: Phil. Trans., 1923, B, 211, p. 351 et seq.

rule out the possibility that the lung may have a secretary function, — especially in view of the fact that in the present year, 1935, two of our most eminent physiologists have restated in considerable detail the case for the vitalistic theory.*

In the last thirty years a great deal of work has been done on the subject of the regulation of respiration. In 1868 Hering and Breuer had shown that one of the functions of the lung was to regulate its own movements, and in 1889 Head had demonstrated very clearly that increase in the volume of the lung tends to inhibit inspiration while decrease in its volume excites inspiration. The work of the 20th century was to show that the movements of the lungs were not governed solely by impulses from these organs. Haldane and Priestley in 1905 discovered that respiration was affected by the carbon dioxide in the blood. Douglas investigated other chemical mechanisms regulating


respiration, and Scott—two years before Douglas—dealt with the nervous factors. In 1919 Sharpey Schäfer showed that animals could live for weeks with both vagi cut, so that respiration can take place without the regulating stimuli from the lungs. This fact was verified by Hammouda and Wilson in 1932. And in 1927 Heymans began an investigation of the part played by the Carotid Sinus in the regulation of respiration.

A subsidiary function of the lung—a function practically ignored by the 18th and 19th century physiologists—is the excretion of water. This function was thoroughly investigated in 1926 by Benedict and Root, who found that in man the water lost by the lungs is approximately equal to that lost

2. Scott: Journal of Physiology, 1908, 37, 301-326.
by the skin, while in animals with few sweat glands – e.g. dogs – the loss of water by the lungs is considerably greater than in man.

Within the last decade the methods of investigation have widened greatly. Not only have many ingenious instruments been devised – by Haldane, Franklin, Gilding, Priestley, and others – to secure a higher degree of accuracy in experimental work, but also, by the steady improvement of radiological technique and the introduction of substances like lipiodol, a valuable new method of investigation has come into existence. New instruments and new methods have not failed to produce results: to mention only four recent volumes, the last six years have produced Dautrebande’s Les Échanges respiratoires (1930), Hess’s Die Regulierung der Athmung (1932), Methods of Air Analysis by Graham and Haldane (1934), and Respiration by Haldane and Priestley (1935).

But to deal with the discoveries of the present day is beyond our scope. Already, in Virgilian phrase, “we have traversed an immense breadth of plain, and it is time
to unyoke the steaming necks of our horses." Before we do so, however, let us glance backwards and endeavour to make out the broad features of the land over which we have been journeying.

Ignoring the minor functions of the lung we may say that the purpose of the organ is "to provide for a supply of oxygen to the tissues and for the escape of the carbon dioxide formed in combustion."* Before this function could be understood the pulmonary circulation, the structure of the lung, and the chemistry of the gases concerned had first to be discovered. Senecio and Harvey laid bare the secrets of the pulmonary circulation, but as late as 1660 practically nothing was known about breathing except the outlines of its muscular mechanism, the fact that cessation of breathing was followed by death, and the fact that breathing was increased by muscular exercise. In the latter part of the 17th century Malpighi and his successors investigated the microscopic structure of the lung, and,

simultaneously, the first steps in the investigation of the chemistry of respiration were taken in England. Boyle, Hooke, and Lower began the quest for oxygen, and then John Mayow— that Keats of Physiology who did his best work before he was 25 and died at the age of 32— grasped the true nature of oxygen, and realised that oxygen passed from the alveoli to the blood and that certain "fumes," formed by "the fermentation of the blood," passed out from the blood to the air. Mayow came very near to solving the whole problem of respiration, but he was in advance of his time: his investigations were forgotten and his work had to be done over again a century later.

In the 18th century the gases concerned in respiration were discovered,—carbon dioxide by Black, hydrogen by Cavendish, and oxygen by Priestley, Scheele, and Lavoisier. The last of these men, Lavoisier, investigated the problem of respiration and showed that carbon and hydrogen combined with oxygen to form carbon dioxide and water; but he made the mistake of assuming that this combination occurred in
the lungs. Magnus, Pflüger, and Evans rectified Lavoisier's error, and so completed the elucidation of the fundamental facts of the physiology of the lungs.

Scores of investigators have made minor discoveries which have altered or increased our knowledge of the physiology of the lungs; scores of investigators still unborn will doubtless continue the process; but in the history of the development of men's knowledge regarding the functions of the lungs the names of Mayow and Lavoisier, and to a lesser extent of Boyle, Hooke, Lower, Black and Magnus, will remain pre-eminent-

"Till, wrapped in flames, in ruin forlorn, Sinks the fabric of the world."