air has been made more and more nearly perfect, the quantity of carbon dioxide in combination has seemed less and less. By far the greatest quantity of the excrementitious carbon dioxide in the blood is extracted by the removal of atmospheric pressure in the most carefully perfected apparatus.

According to Bernard, arterial blood, while an animal is fasting, contains nine to eleven parts per hundred in volume of oxygen. In full digestion, the proportion is raised to seventeen, eighteen or even twenty parts per hundred. The proportion varies in different animals, being much greater, for example, in birds than in mammals. The quantity of carbon dioxide is even more variable than the quantity of oxygen. During digestion there are five to six parts per hundred of carbon dioxide in the arterial blood. During the intervals of digestion this quantity is reduced to almost nothing; and after fasting for twenty-four hours, frequently not a trace is to be discovered.

The quantity of carbon dioxide varies considerably in different parts of the venous system. It is well known that the venous blood coming from some glands is dark, during the intervals of secretion, and nearly as red as arterial blood, during secretion. In the venous blood from the submaxillary gland of a dog, Bernard found 18·07 per cent. of carbon dioxide during repose and 10·14 per cent. during secretion. The blood coming from the muscles is the darkest in the body and contains the greatest quantity of carbon dioxide. The quantity of carbon dioxide is increased in the venous blood during digestion; and it is owing to this that the gas then exists in quantity in the arterial blood. Bearing in mind the fact that the proportion of gases in the arterial and venous blood varies considerably under different conditions of the system and that it is variable in the blood of different veins, the following general statement, taken from Bert (1870), may be accepted as representing the average results obtained up to that time. The most recent results, particularly those obtained by German observers, present no important variations from this average:

	Oxygen.	Carbon dioxide disengaged by a vacuum.	Carbon dioxide in combination.	Carbon dioxide, total.	Nitrogen.	Total gas in volume per 100.
"Arterial blood.	15·03	27·99	1·15	29·14	1·60	45·77
Venous blood..	8·17	31·27	2·38	33·65	1·37	43·19

"If the blood coming from different parts of the body be now examined, it is found that the blood of the hepatic veins is poorer in oxygen and richer in carbon dioxide than the general venous blood; that the blood of the portal vein presents the same characters to a higher degree; that the blood of the muscles in contraction presents the same relations as compared with the blood of muscles in repose or paralyzed; that, on the other hand, the blood of the glands has more oxygen during their activity than during their repose.

"In comparing the venous blood of the right side of the heart with the arterial blood of the left side, it is found that the latter is richer in oxygen and poorer in carbon dioxide. In examining this more closely, it is seen that the difference in the oxygen is greater than in the carbon dioxide; this being in accordance with the well known fact that animals absorb more oxygen than is equivalent to the carbon dioxide exhaled."

These facts coincide with the views which are now held regarding the essential processes of respiration. The blood going to the lungs contains carbon dioxide and but a small proportion of oxygen. In the lungs carbon dioxide is given off, appearing in the expired air, and the oxygen which disappears from the air is carried away by the arterial blood.

Nitrogen of the Blood.—As far as is known, nitrogen has no important office connected with respiration. There is sometimes a slight exhalation of this gas by the lungs, and analyses have demonstrated its existence in solution in the blood. Magnus found generally a larger proportion in the arterial than in venous blood, although in one instance there was a large proportion in the venous blood. It is not absolutely certain whether the nitrogen which exists in the blood be derived from the air or from the tissues. Its almost constant exhalation in the expired air would lead to the supposition that it is produced in small quantity in the system or is supplied by the food. There is no evidence that nitrogen enters into combination with the blood-corpuscles. It exists simply in solution in the blood, which is capable of absorbing about ten times as much as can be absorbed by pure water. Nothing is known with regard to the relations of the free nitrogen of the blood to the processes of nutrition.

Condition of the Gases in the Blood.—It is now generally admitted that the oxygen of the blood exists, not in simple solution, but in a condition of combination with the hæmaglobine of the blood-corpuscles. In studying the composition of the corpuscles, it has been seen that when air is admitted to venous blood, oxygen unites with the hæmaglobine, forming oxyhæmaglobine. Carbon monoxide, which has a great affinity for the corpuscles, displaces almost immediately all the oxygen which the blood contains. When the corpuscles are destroyed, as they may be readily by receiving fresh blood into a quantity of pure water, the red color is instantly changed to black.

The condition under which carbon dioxide exists in the blood has already been considered in connection with the mechanism of its passage from the venous blood into the air-cells. This gas is contained chiefly in the plasma; a small quantity, however, probably exists in the red blood-corpuscles. The greatest part of the carbon dioxide of the plasma is either in simple solution or in a condition of very feeble combination, the exact nature of which is not understood. It has been ascertained that the blood-serum will absorb much more carbon dioxide than is absorbed under similar conditions by pure water. It has been shown, also, that neutral sodium phosphate increases to a remarkable degree the quantity of carbon dioxide that can be absorbed by any liquid. It is probable that a small part of the carbon dioxide of the plasma, which passes into the expired air, is in combination with sodium in the form of sodium bicarbonate.

General Differences in the Composition of Arterial and Venous Blood.—All observers agree that there are certain marked differences in the composition of arterial and venous blood, aside from the proportion of gases. The arterial blood contains less water and is richer in organic and in most inorganic constituents than the venous blood. It also contains a larger proportion of corpuscles. It is more coagulable and offers a larger and firmer clot than the clot of venous blood. The only constituents which are constantly more abundant in venous blood are water and the alkaline carbonates. According to Longet, 10,000 parts of venous blood contained 12·3 parts of carbon dioxide combined, and the same quantity of arterial blood contained but 8·3 parts. The deficiency of water in the blood which comes from the lungs is readily explained by the escape of watery vapor in the expired air.

An important distinction between arterial and venous blood is that the former has a uniform composition in all parts of the arterial system, while the composition of the latter varies very much in the blood coming from different organs. Arterial blood is capable of carrying on the processes of nutrition, while venous blood is not, and it can not even circulate freely in the systemic capillaries.

Relations of Respiration to Nutrition, etc.—It has been demonstrated that all tissues, so long as they retain their absolute integrity of composition, have the property of appropriating oxygen and exhaling carbon dioxide, independently of the presence of blood; and that the arterial blood carries oxygen from the lungs to the tissues, there gives it up, and receives carbon dioxide, which is carried by the venous blood to the lungs, to be exhaled. This fact alone shows that respiration is inseparably connected with the general act of nutrition. Its processes must be studied, therefore, as they take place in the tissues and organs of the body.

Oxygen taken from the air is immediately absorbed by the blood and enters into the composition of the red corpuscles. Part of the oxygen disappears in the red corpuscles themselves, and carbon dioxide is given off. To how great an extent this takes place, it is impossible to say; but it is evident, even from a study of the methods of analysis of the blood for gases, that the property of absorbing oxygen and giving off carbon dioxide, which belongs to the tissues, is possessed as well by the red corpuscles. During life it is not possible to determine how far this takes place in the blood and how far it occurs in the tissues. The theory has been proposed that the respiratory change takes place in the blood as it circulates; but the avidity of the tissues for oxygen and the readiness with which they exhale carbon dioxide leave no room for doubt that much of this change is effected in their substance.

Oxygen, carried by the blood to the tissues, is appropriated and consumed in their substance, together with the nutritive materials contained in the circulating fluid. Physiologists are acquainted with some of the laws which regulate its consumption, but have not been able to ascertain the exact nature of the changes which take place. All that can be said definitely on this point is that oxygen unites with the organic constituents of the body, satisfying the "respiratory sense" and supplying an imperative want which is felt by all animals and which extends to all parts of the organism. After its absorption, oxygen is lost in the processes of nutrition. There is no evidence in

favor of the view that oxygen unites directly with carbonaceous matters in the blood which it meets in the lungs, and by direct union with carbon, forms carbon dioxide.

That carbon dioxide makes its appearance in the blood itself, produced in the red corpuscles, has been abundantly proved by observations already cited, although it is impossible to determine to what extent this takes place during life. It is likewise a product of the physiological wear of the tissues, is absorbed by the blood circulating in the capillaries and is conveyed by the veins to the right side of the heart. It has been shown that its production is not immediately dependent upon the absorption of oxygen, for its formation continues in an atmosphere of hydrogen or of nitrogen. It is most reasonable to consider the carbon dioxide thus formed as a product of excretion. The fact that it may easily be produced artificially, out of the body, does not demonstrate that its formation in the body is as simple as when it is formed by the process of combustion. It may be possible at some future time to produce artificially all the excremetitious principles, as has already been done in the case of urea; but it can not be assumed that the mode of formation of carbon dioxide, as one of the phenomena of nutrition, is precisely the same as when it is made by chemical manipulations.

The Respiratory Sense.

It is generally admitted that there exists in the system what may be regarded as a respiratory sense, which operates upon the respiratory nerve-centre and gives rise to the involuntary movements of respiration; and that this sense is exaggerated by anything which interferes with respiration, and is then conveyed to the brain, where it is appreciated as dyspnœa and finally as the sense of suffocation. An exaggeration of the respiratory sense constitutes a sense of oppression, which is referred to the lungs; but it can not be assumed, from sensations only, that the sense of want of air is really situated in the lungs.

At the present day it is hardly necessary to discuss the views of those who attributed the sense of want of air, at least in its exaggerated form, to an accumulation of carbon dioxide in the lungs (Marshall Hall), distention of the right cavities of the heart (Bérard), or to impressions conveyed to the medulla oblongata, exclusively by the pneumogastric nerves. These theories have long since been disproved and are now merely of historical interest. Volkmann, in 1841, advanced the view that this sense is dependent upon a deficiency of oxygen in the tissues, producing an impression which is conveyed to the medulla oblongata by the nerves of general sensibility. By a series of experiments, this observer disproved the view that the respiratory sense always originates in the lungs and is transmitted by the pneumogastric nerves; and by exclusion, he located it in the general system. In a series of experiments (Flint, 1861) the following facts, some of which had been previously noted, were observed:

The chest was opened in a living animal, artificial respiration was carefully performed, inflating the lungs sufficiently but cautiously and taking care to change the air in the bellows every few moments. So long as this was continued, the animal made no respiratory effort; showing that for the time the respiratory sense was abolished. This was little more than a repetition of the classical experiment of Robert Hook, an account of which was published in 1664.

When the artificial respiration was interrupted, the respiratory muscles were thrown into contraction, and the animal made regular, and at last violent efforts. An artery was then opened and the color of the blood was noted. It was observed that the respiratory efforts began only when the blood in the vessel became dark. When artificial respiration was resumed, the respiratory efforts ceased only when the blood became red in the arteries.

While artificial respiration was being regularly performed, a large artery was opened and the system was drained of blood. When the hæmorrhage had proceeded to a certain extent, the animal made respiratory efforts, which became more and more violent, until they terminated, just before death, in general convulsions.

These facts, which may be successively observed in a single experiment, remained precisely the same when both pneumogastric nerves had been divided in the neck.

The conclusion which may legitimately be drawn from the above-mentioned facts is that the respiratory sense does not always and necessarily originate in the lungs, for it operates when the lungs are regularly filled with pure air, if the system be drained of the oxygen-carrying fluid.

A similar conclusion was arrived at by Rosenthal (1862) and by Pflüger (1868). Pflüger produced asphyxia in dogs by causing them to respire pure nitrogen. In his experiments, he analyzed the blood after thirty seconds and after one minute of inhalation of nitrogen. He found a great diminution in oxygen with very slight increase in carbon dioxide at the end of thirty seconds. After one minute the oxygen was reduced from 14·35 per cent. in volume to 0·2 per cent., and the carbon dioxide from 36·9 to 29·9. As a conclusion he stated that "no one, therefore, can be of the opinion that dyspnœa and asphyxia in breathing indifferent gases are connected with the accumulation of carbon dioxide."

In 1877 the experiments made in 1861 were repeated and extended (Flint). The later experiments were made upon dogs, in the following way: The animals were brought under the influence of ether, the chest was opened and artificial respiration was carried on by means of a bellows fixed in the trachea. The great vessels given off from the arch of the aorta were isolated so that they could be separately constricted at will. In a number of experiments upon different animals, the innominate artery and the left subclavian were constricted, and the animal began to make respiratory efforts about two minutes after, although artificial respiration was kept up constantly and efficiently. The animals made no respiratory efforts when the vessels given off from the arch of the aorta were left free and when the aorta was tied in the chest, which cut off the supply of blood from the trunk and the lower extremities. In the experiments in which the vessels going to the head and

upper extremities were constricted, the respiratory efforts always ceased when the vessels were freed.

The object of these experiments was to study the effects of cutting off the supply of oxygenated blood from different parts. It may be assumed that the respiratory nervous centre is in the medulla oblongata, and an attempt was made to devise some means of cutting off the arterial supply from this part. Animals respire when all of the encephalic centres have been destroyed except the medulla oblongata, so that it is improbable that cutting off the supply of blood from the brain would affect the muscles of respiration, provided that artificial respiration were efficiently maintained. Blood may be supplied to the medulla oblongata by the internal carotids, which are connected with the circle of Willis, by the vertebral arteries, which unite to form the basilar artery, and perhaps by other vessels; but it is certain that if all the arteries given off from the arch of the aorta be tied, the medulla must be deprived of oxygenated blood.

In one experiment, the innominate artery and the left subclavian artery were constricted, and the animal made respiratory efforts in two minutes and eight seconds, notwithstanding that artificial respiration was kept up.

In another experiment, the same vessels were constricted, and the animal made respiratory efforts in two minutes and five seconds.

In a third experiment, both subclavian arteries and both carotids were constricted, and the animal made respiratory efforts in two minutes and seven seconds. Both vertebral arteries and both carotids were constricted, and the animal made no respiratory efforts for five minutes; but respiratory efforts were made in one minute and thirty-five seconds after both subclavians had been constricted in addition to the vertebrals and carotids.

It seems from these experiments, that in order to induce respiratory efforts in an animal under the influence of ether and with the lungs supplied with air by artificial respiration, either the innominate artery and the left subclavian artery, or both subclavians, both carotids and both vertebral arteries, must be tied. In other words, according to the view taken of the cause of these respiratory efforts, the supply of blood to the medulla oblongata can not be cut off completely except by tying all the vessels given off from the arch of the aorta.

These observations, taken in connection with the experiments of 1861, lead to the conclusion that the sense of want of air, under certain conditions, is due to a want of circulation of oxygenated blood in the medulla oblongata. This view has been advanced by some writers, but it has lacked the positive experimental proof afforded by the experiments of 1877.

If the sense of want of air be regarded as due, under certain conditions, to a deficiency of oxygen in the medulla oblongata—which can hardly be doubted—it becomes an important question to determine whether the normal respiratory movements be actually reflex in their character or whether they be due to direct excitation of the nerve-cells in the respiratory centre.

It is difficult to account for the phenomena observed in experiments in which the pneumogastrics are divided or stimulated, without assuming that these nerves sometimes—and possibly always, in tranquil respiration—convey an impression to the respiratory nervous centre, which gives rise to the ordinary automatic and periodical action of the muscles of inspiration. If such an impression be conveyed from the lungs by the afferent fibres of the pneumogastrics, it could not operate when both pneumogastrics are divided in the neck. This operation, as is well known, profoundly affects the respiratory movements. After division of both nerves, the respirations become slow and unusually deep, without, as a rule, any evidence of respiratory distress. In dogs, the number of respirations often falls to four or five per minute, and their nervous mechanism seems to be modified. Any respiratory distress that occurs is due to the arrest of the respiratory movements of the larynx, and not to an exaggeration of the sense of want of air. When a feeble Faradic current is passed through the nerves, the respiratory movements are increased in frequency, but the movements are arrested by a relatively powerful current. This action is reflex.

In view of all the experimental facts bearing upon the question, it is probable that the respiratory movements are sometimes reflex and sometimes due to direct excitation of the cells of the respiratory centre by the absence of oxygen.

In perfectly normal and tranquil respiration, an impression is probably conveyed from the lungs to the respiratory centre by the pneumogastrics, which stimulates this centre to excite movements of inspiration. This is probably due to a gradual and progressive change in the character of the contents of the air-cells, although experiments are wanting to show the exact mechanism of this process.

When this reflex action is abolished, as by section of both pneumogastrics in the neck, the respiratory centre is stimulated only when the deficiency in the supply of oxygen becomes considerable. This excitation of the respiratory centre is direct. It requires a certain time for its operation, and this accounts for the slow respirations in animals after the pneumogastrics have been divided. Under certain physiological conditions, this direct stimulation may be added to the impression conveyed by the pneumogastrics, and it is probable that this always occurs in dyspnœa.

Sense of Suffocation.—The respiratory sense must not be confounded with the sense of distress from want of air, and its extreme degree, the sense of suffocation. The first is not a sensation, but an impression made upon the medulla oblongata, giving rise to involuntary respiratory movements. The necessities for oxygen on the part of the system regulate the supply of air to the lungs. Once in every seven or eight respirations, or when the respiratory movements are restricted under the influence of depressing emotions, an involuntary, deep or sighing inspiration is made, for the purpose of changing the air in the lungs more completely. The increased consumption of oxygen and a certain degree of interference with the mechanical process of respiration during violent muscular exercise put one "out of breath," and for a time the respiratory movements are exaggerated. This is perhaps the first physiological way in which the want of air is appreciated by the senses. A deficiency in hæmatosis, either from a vitiated atmosphere, mechanical obstruction in the air-passages or grave trouble in the general circulation, produces all grades of sensations, from the slight oppression which is felt in a crowded room, to the intense distress of suffocation. When hæmatosis is but slightly interfered with, only an indefinite sense of oppression is experienced, and the respiratory movements are a little increased, the most marked effect being an increase in the number and extent of sighing inspirations.

Respiratory Efforts before Birth.

It is generally admitted that one of the most important uses of the placenta, and the one which is most immediately connected with the life of the fœtus, is a respiratory interchange of gases, analogous to that which takes place in the gills of aquatic animals. The placental villi are bathed in the blood of the uterine sinuses, and this is the only way in which the fœtal blood can receive oxygen. Legallois observed a bright-red color in the blood of the umbilical vein; and on alternately compressing and releasing the vessel, he saw the blood change in color successively from red to dark and from dark to red. Zweifel has demonstrated the presence of oxyhæmaglobine in the blood of the umbilical vessels by means of the spectroscope, thus showing that it contains oxygen. As oxygen is thus adequately supplied to the system, the fœtus is in a condition similar to that of the animals in which artificial respiration was effectually performed. The want of oxygen is fully met, and therefore no respiratory efforts take place. Respiratory movements will take place, however, even in very young animals, when there is a deficiency of oxygen in the system. It has been observed that the liquor amnii occasionally finds its way into the respiratory passages of the fœtus, where it could enter only during efforts at respiration. Winslow, in the latter part of the last century, first noticed respiratory efforts in the fœtuses of cats and dogs in the uterus of the mother during life; and many others have observed that when fœtuses are removed from vascular connection with the mother, they make vigorous efforts at respiration. After the death of the mother, the fœtus always makes a certain number of distinct and unmistakable respiratory efforts, which follow each other at regular intervals.

From what has been experimentally demonstrated with regard to the seat and cause of the respiratory sense after birth, it is evident that want of oxygen is the cause of respiratory movements in the fœtus. When the circulation in the maternal portion of the placenta is interrupted from any cause, or when the blood of the fœtus is obstructed in its course to and from the placenta, the impression due to want of oxygen is made upon the medulla oblongata, and efforts at respiration are the result.

Cutaneous Respiration.

Respiration by the skin, although very important in many of the lower forms of animals, is inconsiderable in the human subject and is even more insignificant in animals covered with hair or feathers; still, an appreciable