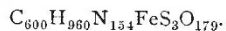


the Itany and that of the Camopy. Starting by the Maroni, M. Coudreau, after having gone up the Itany and explored the region which it waters, came down to the coast by Maronimicrique, which is a very large tributary of the Maroni River. M. Coudreau is the first Frenchman who has passed a consecutive winter and summer in the Tumuc-Humac Mountains, and though he did not himself suffer very much from the effects of the expedition, the same cannot be said of his companions, as the only European who accompanied him was brought near to death's door by fever, from which most of the natives also suffered. M. Coudreau escaped with nothing worse than rheumatism, and he says that the climate of the Western Tumuc-Humac is not bad. The result of 1200 observations taken by him puts the mean temperature at 70°, and the country is a magnificent one; but the difficulty of reaching it is very great owing to the uncertainty of communication with the coast. M. Coudreau and his companions, when they had exhausted their provisions, had to go and live out in the open with the Indians, leading the same kind of existence, and depending for food upon the game, fish, and fruit that they could shoot, fish, and gather. For eight months M. Coudreau lived the regular native life, and he had become so accustomed to it that he was very popular with the Rucayennes, whose language he had learned to speak, and he induced the *pamenchi* (captain) of the tribe and four of his lieutenants to accompany him to Cayenne, where their arrival created a great sensation, as the people of the town did not believe in their existence. M. Gerville-Réache, the Governor of the colony, received them with great hospitality, and made them several presents. The most important fact brought out by M. Coudreau is the existence in Upper Guiana, which is acknowledged French territory, of sixteen new Indian tribes, forming a group of at least 20,000 persons; and these Indians are not, as was supposed, mere nomads, living upon the produce of their guns and fishing-nets, but are sedentary in their habits, and have attained a certain degree of civilization. M. Coudreau is about to start on a fresh expedition to the Appruague and the Oyapack, and does not expect to get back before next spring.

THE GASES OF THE BLOOD.¹

II.

THE next step was the discovery of the important part performed in respiration by the colouring matter of the red blood corpuscles. Chemically, these corpuscles consist of about 30 or 40 per cent. of solid matter. These solids contain only about 1 per cent. of inorganic salts, chiefly those of potash; whilst the remainder are almost entirely organic. Analysis has shown that 100 parts of dry organic matter contain of hæmoglobin, the colouring matter, no less than 90·54 per cent.: of proteid substances, 8·67; of lecithin, 0·54; and of cholesterine, 0·25. The colouring matter, hæmoglobin, was first obtained in a crystalline state by Funke in 1853, and subsequently by Lehmann. It has been analyzed by Hoppe-Seyler and Carl Schmidt, with the result of showing that it has a perfectly constant composition. Hoppe-Seyler's analysis first appeared in 1868. It is now well known to be the most complicated of organic substances, having a formula, as deduced, from the analyses I have just referred to, by Preyer (1871), of



In 1862, Hoppe-Seyler noticed the remarkable spectrum produced by the absorption of light by a very dilute solution of blood. Immediately thereafter, the subject was investigated by Prof. Stokes, of Cambridge, and communicated to the Royal Society in 1864. If white light be transmitted through a thin stratum of blood, two distinct absorption bands will be seen. One of these bands next D is narrower than the other, has more sharply defined edges, and is undoubtedly blacker. "Its centre," as described by Dr. Gamgee ("Physiological Chemistry," p. 97), "corresponds with wave-length 579," and it may conveniently be distinguished as the absorption band, *a*, in the spectrum of oxyhæmoglobin. The second of the absorption bands—that is, the one next to E—which we shall designate *β*, is broader, has less sharply defined edges, and is not so

dark as *a*. Its centre corresponds approximately to wave-length 553·8. On diluting very largely with water, nearly the whole of the spectrum appears beautifully clear, except where the two absorption bands are situated. If dilution be pursued far enough, even these disappear; before they disappear they look like faint shadows obscuring the limited part of the spectrum which they occupy. The last to disappear is the band *a*. The two absorption bands are seen most distinctly when a stratum of 1 cm. thick of a solution containing 1 part of hæmoglobin in 1000 is examined; they are still perceptible when the solution contains only 1 part of hæmoglobin in 10,000 of water."

Suppose, on the other hand, we begin with a solution of blood in ten times its volume of water; we then find that such a solution cuts off the more refrangible part of the spectrum, leaving nothing except the red, "or, rather, those rays having a wave-length greater than about 600 millionths of a millimetre." On diluting further, the effects, as well described by Prof. Gamgee, are as follows:—"If now the blood solution be rendered much more dilute, so as to contain 8 per cent. of hæmoglobin, on examining a spectrum 1 centimetre wide the spectrum becomes distinct up to Fraunhofer's line D (wave-length 589)—that is, the red, orange, and yellow are seen, and in addition also a portion of the green, between *b* and F. Immediately beyond D, and between it and *b*, however (between wave-lengths 595 and 518), the absorption is intense."

These facts were observed by Hoppe-Seyler. Prof. Stokes made the very important contribution of observing that the spectrum was altered by the action of reducing agents. Hoppe-Seyler had observed that the colouring matter, so far as the spectrum was concerned, was unaffected by alkaline carbonates, and caustic ammonia, but was almost immediately decomposed by acid; and also slowly by caustic fixed alkalies, the coloured product of decomposition being hæmatin, the spectrum of which was known. Prof. Stokes was led to investigate the subject from its physiological interest, as may be observed on quoting his own words in the classical research already referred to. "But it seemed to me to be a point of special interest to inquire whether we could imitate the change of colour of arterial into that of venous blood, on the supposition that it arises from reduction."

He found that—

"If to a solution of proto-sulphate of iron enough tartaric acid be added to prevent precipitation by alkalies, and a small quantity of the solution, previously rendered alkaline by either ammonia or carbonate of soda, be added to a solution of blood, the colour is almost instantly changed to a much more purple-red as seen in small thicknesses, and a much darker red than before as seen in greater thickness. The change of colour which recalls the difference between arterial and venous blood is striking enough, but the change in the absorption spectrum is far more decisive. The two highly characteristic dark bands seen before are now replaced by a single band, somewhat broader and less sharply defined at its edges than either of the former, and occupying nearly the position of the bright band separating the dark bands of the original solution. The fluid is more transparent for the blue and less so for the green than it was before. If the thickness be increased till the whole of the spectrum more refrangible than the red be on the point of disappearing, the last part to remain is green, a little beyond the fixed line *b*, in the case of the original solution, and blue some way beyond F, in the case of the modified fluid."

From these observations, Prof. Stokes was led to the important conclusion that—

"The colouring matter of blood, like indigo, is capable of existing in two states of oxidation, distinguishable by a difference of colour and a fundamental difference in the action on the spectrum. It may be made to pass from the more to the less oxidized by the action of suitable reducing agents, and recovers its oxygen by absorption from the air."

To the colouring matter of the blood Prof. Stokes gave the name of crurine, and described it in its two states of oxidation as scarlet crurine and purple crurine. The name hæmoglobin, given to it by Hoppe-Seyler, is generally employed. When united with oxygen it is called oxyhæmoglobin, and when in the reduced state it is termed reduced hæmoglobin, or simply hæmoglobin.

The spectroscopic evidence is, therefore, complete. Hoppe-Seyler, Hüfner, and Preyer have shown also that pure crystallized hæmoglobin absorbs and retains in combination a quantity of oxygen equal to that contained in a volume of blood holding the same amount of hæmoglobin. Thus, 1 gramme of hæmoglobin absorbs 1·56 cubic centimetre of oxygen at 0° C. and 760 milli-

¹ Address to the British Medical Association at its annual meeting at Glasgow. Delivered on August 10 in the Natural Philosophy class-room, University of Glasgow, by John Gray McKendrick, M.D., LL.D., F.R.S.S.L. and E., F.R.C.P.E., Professor of the Institutes of Medicine in the University of Glasgow. Continued from p. 382.

² Dr. Gamgee gives the measurements of the wave-lengths in millionths, not in ten-millionths of a millimetre.

metres pressure; and, as the average amount of hæmoglobin in blood is about 14 per cent., it follows that $1.56 \times 14 = 21.8$ cubic centimetres of oxygen would be retained by 100 cubic centimetres of blood. This agrees closely with the fact that about 20 volumes of oxygen can be obtained from 100 volumes of blood. According to Pflüger, arterial blood is saturated with oxygen to the extent of nine-tenths, while Hüfner gives the figure at fourteen-fifteenths. By shaking blood with air, its oxygen contents can be increased to the extent of from 1 to 2 volumes per cent.

These important researches, the results of which have been amply corroborated, have given an explanation of the function of the red blood corpuscles as regards respiration. The hæmoglobin of the venous blood in the pulmonary artery absorbs oxygen, becoming oxyhæmoglobin. This is carried to the tissues, where the oxygen is given up, the hæmoglobin being reduced. Thus, the colouring matter of the red blood corpuscles is constantly engaged in conveying oxygen from the lungs to the tissues. Probably the union of hæmoglobin with oxygen, and its separation from it, are examples of dissociation—that is, of a chemical decomposition or synthesis, effected entirely by physical conditions; but data regarding this important question are still wanting. If the union of oxygen with the colouring matter is an example of oxidation, it must be attended with the evolution of heat, but, so far as I know, this has not been measured. In co-operation with my friend, Mr. J. T. Bottomley, I have recently been able to detect, by means of a thermo-electric arrangement, a rise of temperature on the formation of oxyhæmoglobin. We mean to prosecute our researches in this direction. If heat were produced in considerable amount, the arterial blood returned from the lungs to the left auricle would be hotter than the blood brought to the right auricle by the veins. This, however, is not the case, as the blood on the right side of the heart is decidedly warmer than the blood on the left—a fact usually accounted for by the large influx of warm blood coming from the liver. The heat-exchanges in the lungs are of a very complicated kind. Thus, heat will be set free by the formation of oxyhæmoglobin; but, on the other hand, it will be absorbed by the escape of carbonic acid, and by the formation of aqueous vapour, and a portion will be used in heating the air of respiration. The fact that the blood in the left auricle is colder than that of the right auricle is, therefore, the result of a complicated series of heat-exchanges, not easy to follow.

Our knowledge as to the state of the carbonic acid in the blood is not so reliable. In the first place, it is certain that almost the whole of the carbonic acid which may be obtained exists in the plasma. Defibrinated blood gives up only a little more carbonic acid than the same amount of serum of the same blood. Blood serum gives up to the vacuum about 30 volumes per cent. of carbonic acid; but a small part—according to Pflüger, about 6 volumes per cent.—is given up only after adding an organic or mineral acid. This smaller part is chemically bound, just as carbonic acid is united to carbonates, from which it can be expelled only by a stronger organic or mineral acid. The ash of serum yields about one-seventh of its weight of sodium; this is chiefly united to carbonic acid to form carbonates, and a part of the carbonic acid of the blood is united to those salts. It has been ascertained, however, that defibrinated blood, or even serum containing a large number of blood corpuscles, will yield a large amount of carbonic acid, even without the addition of an acid. Thus, defibrinated blood will yield 40 volumes per cent. of carbonic acid—that is, 34 volumes which would be also given up by the serum of the same blood (without an acid), and 6 volumes which would be yielded after the addition of an acid. Something, therefore, exists in defibrinated blood which acts like an acid in the sense of setting free the 6 volumes of carbonic acid. Possibly the vacuum may cause a partial decomposition of a portion of the hæmoglobin, and, as suggested by Hoppe-Seyler, acid substances may thus be formed.

But what is the condition of the remaining 30 volumes per cent. of carbonic acid which are obtained by the vacuum alone? A portion of this is probably simply absorbed by the serum; this part escapes in proportion to the decrease of pressure, and it may be considered to be physically absorbed. A second part of this carbonic acid must exist in chemical combination, as is indicated by the fact that blood serum takes up far more carbonic acid than is absorbed by pure water. On the other hand, this chemical combination is only a loose one, because it is readily dissolved by the vacuum. There can be no doubt that a part of this carbonic acid is loosely bound to carbonate of soda, Na_2CO_3 , in the serum,

probably to acid carbonate of soda, NaHCO_3 . This compound exists only at a certain pressure. On a fall of pressure, it decomposes into sodium carbonate and carbonic acid, the latter becoming free. A third part of this carbonic acid is probably loosely bound chemically to disodium phosphate, Na_2HPO_4 , a salt which also occurs in the blood serum. Fernet has shown that it binds two molecules of carbonic acid to one molecule of phosphoric acid. This salt occurs in considerable quantity only in the blood of Carnivora and Omnivora, while in that of Herbivora, such as in the ox and calf, only traces exist. It cannot be supposed in the latter instances to hold much carbonic acid in chemical combination. There must exist, therefore, other chemical substances for the attachment of the carbonic acid of the blood, and it has been suggested that a part may be connected with the albumin of the plasma.

According to Zuntz, the blood corpuscles themselves retain a part of the carbonic acid, as the total blood is able to take up far more carbonic acid out of a gaseous mixture rich in carbonic acid, or consisting of pure carbonic acid, than can be absorbed by the serum of the same quantity of blood. No compound, however, of carbonic acid with the blood corpuscles is known.

The nitrogen which is contained in the blood to the amount of from 1.8 to 2 volumes per cent., is probably simply absorbed, for even water is able to absorb to 2 volumes per cent. of this gas.

If we then regard the blood as a respiratory medium having gases in solution, we have next to consider what is known of the breathing of the tissues themselves. Spallanzani was undoubtedly the first to observe that animals of a comparatively simple type used oxygen and gave up carbonic acid. But he went further, and showed that various tissues and animal fluids, such as the blood, the skin, and portions of other organs, acted in a similar way. These observations were made before the beginning of the present century, but they appear to have attracted little or no attention until the researches of Georg Liebig on the respiration of muscle, published in 1850. He showed that fresh muscular tissue consumed oxygen and gave up carbonic acid. In 1856, Matteucci made an important advance, by observing that muscular contraction was attended by an increased consumption of oxygen, and an increased elimination of carbonic acid. Since then, Claude Bernard and Paul Bert, more especially the latter, have made numerous observations regarding this matter. Paul Bert found that muscular tissue has the greatest absorptive power. Thus we arrive at the grand conclusion that the living body is an aggregate of living particles, each of which breathes in the respiratory medium passing from the blood.

As the blood, containing oxygen united with the colouring matter (hæmoglobin), passes slowly through the capillaries, fluid matter transudes through the walls of the vessels, and bathes the surrounding tissues. The pressure or tension of the oxygen in this fluid being greater than the tension of the oxygen in the tissues themselves, in consequence of the oxygen becoming at once a part of the living protoplasmic substance, oxygen is set free from the hæmoglobin, and is appropriated by the living tissues, becoming part of their protoplasm. Whilst alive, or at all events whilst actively discharging their functions, as in the contraction of a muscle, or in those changes we term secretion in a cell, the living protoplasm undergoes rapid decompositions, leading to the formation of comparatively simple substances. Amongst these is carbonic acid. As it has been ascertained that the tension of the carbonic acid in the lymph is less than its tension in venous blood, it is difficult at first sight to account for the absorption of carbonic acid by venous blood; but its tension is higher than that of carbonic acid in arterial blood, and it must be remembered that the lymph has had the opportunity, both in the connective tissue and in the lymphatic vessels, of modifying its tension by close contact with arterial blood. Strassburg fixes the tension of the carbonic acid in the tissues as equal to 45 mm. of mercury, while that of the venous blood is only 41 mm. We may assume that as the carbonic acid is set free, it is absorbed by the blood, uniting loosely with the carbonates and phosphates of that fluid, thus converting it from the arterial into the venous condition. This constitutes respiration of tissue.

In connection with the respiration of tissue, as determined by the analysis of the blood gases and of the gases of respiration, there arises the interesting question of the ratio between the amount of oxygen absorbed and the amount of carbonic acid produced, and very striking contrasts among animals have thus been determined. Thus in Herbivora the ratio of the oxygen absorbed to the carbonic acid produced, or the respiratory quotient, as it is termed by Pflüger, $\frac{\text{CO}_2}{\text{O}}$ amounts to from 0.7 to 1.0, while in

Carnivora it is from 0.75 to 0.8. Omnivora, of which man may be taken as the example, come between $\frac{CO_2}{O} = 0.87$. The quotient is greater in proportion to the amount of carbohydrate in the diet, whether the animals are Carnivora, Herbivora, or Omnivora.

The respiratory quotient becomes the same, about 0.75, in starving animals, a proof that the oxidations are kept up at the cost of the body itself, or, in other words, the starving animal is carnivorous. The intensity of respiration in different animals is well shown in the following table, in which the amount of oxygen used is given per kilogramme of body-weight per hour (Dr. Immanuel Munk, "Physiologie des Menschen und der Säugethiere," 1888, p. 82).

Animal.	O in grammes.	Respiratory Quotient, $\frac{CO_2}{O}$.
Cat	1.007	0.77
Dog	1.183	0.75
Rabbit	0.918	0.92
Hen	1.300	0.93
Small singing birds ...	11.360	0.78
Frog	0.084	0.63
Cockchafer	1.019	0.81
Man	0.417	0.78
Horse	0.563	0.97
Ox	0.552	0.98
Sheep	0.490	0.98

Smaller animals therefore have, as a rule, a greater intensity of respiration than larger ones. In small singing birds the intensity is very remarkable, and it will be seen that they require ten times as much oxygen as a hen. On the other hand, the intensity is low in cold-blooded animals. Thus a frog requires 135 times less oxygen than a small singing bird. The need of oxygen is therefore very different in different animals. Thus a guinea-pig soon dies with convulsions in a space containing a small amount of oxygen, while a frog will remain alive for many hours in a space quite free of oxygen. It is well known that fishes and aquatic animals generally require only a small amount of oxygen, and this is in consonance with the fact that sea-water contains only small quantities of this gas. Thus, according to the elaborate researches of my friend, Prof. Dittmar, on the gases of the sea-water brought home by the *Challenger* Expedition, collected in many parts of the great oceans, and from varying depths:—"The ocean can contain nowhere more than 15.6 c.c. of nitrogen, or more than 8.18 c.c. oxygen per litre; and the nitrogen will never fall below 8.55 c.c. We cannot make a similar assertion in regard to the oxygen, because its theoretical minimum of 4.30 c.c. per litre is liable to further diminution by processes of life and putrefaction and processes of oxidation" (Dittmar, Proceedings of Phil. Soc. of Glasgow, vol. xvi. p. 61). As a matter of fact, a sample of water from a depth of 2875 fathoms gave only 0.6 c.c. per litre of oxygen, while one from a depth of 1500 fathoms gave 2.04 c.c. per litre. Taking 15° C. as an average temperature, one litre of sea-water would contain only 5.31 c.c. of dissolved oxygen—that is, about 0.5 c.c. in 100 c.c. Contrast this with arterial blood, which contains 20 c.c. of oxygen in 100 c.c. of blood, or there are about forty times as much oxygen in arterial blood as in sea-water. At great depths the quantity of oxygen is very much less, and yet many forms of life exist at these great depths. Fishes have been dredged from a depth of 2750 fathoms, where the amount of oxygen was probably not so much as 0.06 c.c. per 100 c.c., or 300 times less than that of arterial blood. Making allowance for the smaller quantity of oxygen in the blood of a fish than that of a mammal, it will still be evident that the blood of the fish must contain much more oxygen than exists in the same volume of sea-water. No doubt we must remember that the water is constantly renewed, and that the oxygen in it is in the state of solution, or, in other words, in a liquid state. But the question remains, where do these deep-sea creatures obtain the oxygen? Probably by a method of storage. Biot has found in the swimming-bladder of such fishes 70 volumes per cent. of pure oxygen, a gas in which a glowing splinter of wood is relit. This oxygen probably oxygenates the blood of the fish when it plunges into the dark and almost airless depths of the ocean.

Aquatic breathers, however, if they live in a medium containing little oxygen, have the advantage that they are not troubled with free carbonic acid. One of the most striking facts discovered by the *Challenger* chemists is that sea-water contains no free

carbonic acid, except in some situations where the gas is given off by volcanic action from the crust of the earth forming the sea-bed. In ordinary sea-water there is no free carbonic acid, because any carbonic acid formed is at once absorbed by the excess of alkaline base present. Thus the fish breathes on the principle of Fleuss's diving apparatus, in which the carbonic acid formed is absorbed by an alkaline solution. There is nothing new under the sun. The fish obtains the oxygen from the sea-water, no doubt, by the chemical affinity of its hæmoglobin, which snatches every molecule of oxygen it may meet with, while it gets rid of its carbonic acid easily, because there is not only no tension of carbonic acid in the sea-water to prevent its escape, but there is always enough of base in the sea-water to seize hold of the carbonic acid the moment it is formed. If we could get rid of the carbonic acid of the air of expiration as easily, we could live in an atmosphere containing a much smaller percentage of oxygen.

I have now placed before you the generally accepted doctrines regarding the chemical and physical problems of respiration. But one has only to examine them closely to find that there are still many difficulties in the way of a satisfactory explanation of the function. For example, is the union of hæmoglobin with oxygen a chemical or a physical process? If oxyhæmoglobin is a chemical substance, how can the oxygen be so readily removed by means of the air-pump? On the other hand, if it is a physical combination, why is the oxygen not absorbed according to the law of pressure? It is important to note that, as a matter of fact, hæmoglobin absorbs a quantity of oxygen nearly constant for ordinary temperatures, whatever may be the amount of oxygen present in the mixture of gases to which it is exposed. This is true so long as the amount of oxygen does not fall below a certain minimum, and it clearly points to the union of the hæmoglobin with the oxygen being a chemical union. Suppose we diminish the amount of oxygen in the air breathed, the partial pressure of the gas is of course also diminished, but it is evident that we might diminish the total pressure instead of diminishing the amount of oxygen. To avoid difficulties in respiration, when one is obliged to breathe an air deficient in oxygen, we ought to increase the pressure at which the air is breathed; and, on the other hand, to avoid danger in breathing air under a low pressure, we ought theoretically to increase the richness of the air in oxygen. Thus, with a pressure of 760 mm. the air should contain, as it normally does, 21 per cent. of oxygen, while with a pressure of 340 mm. it should contain 46 per cent., and with a pressure of 250 mm. it should contain as much as 63 per cent. On this basis a pressure of 5 atmospheres should be associated with an atmosphere containing about 3 per cent. of oxygen. By increasing the pressure, we increase the quantity of oxygen by weight in a given volume.

The explanation is that in all of these cases the partial pressure of the oxygen is nearly the same—that is, not far from 157 mm. of mercury, and the general law is that for all kinds of breathing the pressure of the oxygen should be nearly that of the oxygen in ordinary atmospheric air. Whilst the absorption of oxygen by the hæmoglobin has nothing directly to do with the pressure, it is striking that any atmosphere contains enough oxygen by weight for the hæmoglobin in the blood, when the partial pressure of the oxygen is near 157 mm. On each side of this median line life can be supported with considerable differences of pressure. Thus the pressure may be gradually reduced until the point of the dissociation of oxyhæmoglobin is reached—that is to say, down to about $\frac{1}{10}$ of an atmosphere. On the other hand, animals may breathe an atmosphere containing two or three times the normal amount of oxygen without appearing to be affected. This was first noticed by Regnault and Reiset, and the observation has been much extended by Paul Bert. The latter distinguished physiologist found that an increase even up to 8 or 10 atmospheres did not produce any apparent effect, but on reaching the enormous pressure of 20 atmospheres, death, with severe tetanic convulsions, was the result. He also showed that the additional increment of oxygen absorbed by the blood under the influence of each atmosphere of added pressure was very small. Thus, with a pressure of 1 atmosphere the amount of oxygen absorbed by the blood was about 20 per cent. by volume, a pressure of 2 atmospheres caused an increase of only 0.9 per cent., of 3 atmospheres 0.7 per cent., of 4 atmospheres 0.6 per cent., of 5 atmospheres 0.5 per cent., of 6 atmospheres 0.2 per cent., of 7 atmospheres 0.2 per cent., of 8 atmospheres 0.1 per cent., of 9 atmospheres 0.1 per cent., and of 10 atmospheres 0.1 per cent. Thus from 1 atmosphere to 10 atmospheres the increase was only to the extent of 3.4 per cent.,

so that the blood now contained 23·4 per cent. by volume instead of 20 per cent. These facts indicate that when all the hæmoglobin has been satisfied with oxygen it becomes indifferent, within limits, to any additional oxygen that may be forced into the blood under pressure, and thus the blood of animals breathing an atmosphere richer in oxygen than ordinary air is not more highly oxygenated than normal blood. The practical result also follows that it is of no use in the treatment of disease to cause patients to breathe an atmosphere richer in oxygen than ordinary air, because, at ordinary atmospheric pressure, no more oxygen can thus be caused to enter the blood, and if it be desirable to hyperoxygenate the blood, this can only be done by breathing oxygen, under a pressure of three or four atmospheres, in a chamber in which the body of the patient is subjected to the same pressure.

In this connection it is important to notice the enormous absorptive surface for oxygen presented by the red blood corpuscles of man. There are about 5,000,000 red corpuscles in each cubic millimetre. Each corpuscle has a superficial area of 0·000128 square millimetre. Taking the blood in the body of a man of average size at 4·5 litres, that is 4,500,000 cubic millimetres, the number of corpuscles is about 22,500,000,000,000, and this would give a superficial area of 2,880,000,000 square millimetres, or 2880 square metres, or about 3151 square yards—that is to say, the absorptive area of the blood corpuscles is equal to that of a square having each side about 56 yards. The hæmoglobin in a red blood corpuscle amounts to about $\frac{1}{3}$ of its weight. The blood of a man of average size may be taken at 4536 grammes, or about 10 pounds. Such blood contains about 13·083 per cent. of hæmoglobin, and 4536 grammes will contain about 593 grammes of hæmoglobin, or about $1\frac{1}{2}$ pound. As regards the iron, which is supposed to be an essential constituent of hæmoglobin, 100 grammes of blood contain 0·0546 gramme. It follows that the total amount, 4536 grammes, contain about 2·48 grammes, or nearly 39 grains. Twenty-five minims of the tinctura ferri perchloridi contain about 1 grain of pure iron, so it will be seen that not many doses are required to introduce into the body an amount of iron as large as exists in the whole of the blood.

The absorption of oxygen, therefore, probably takes place as follows: the inspired air is separated in the alveoli of the lung by delicate epithelial cells and the endothelial wall of the pulmonary capillaries from the blood which circulates in the latter. The exchange of gas takes place through these thin porous membranes, so that the velocity of the transit must be practically instantaneous. As the oxygen is bound loosely to the hæmoglobin of the corpuscles, the laws of diffusion can have only a secondary influence on its passage, and only so far as it has to pass into the plasma so as to reach the blood-corpuscles. The plasma will absorb, at 35° C., about 2 volumes per cent., if we take the coefficient absorption of the plasma as equal to that of distilled water. Many of the blood corpuscles of the pulmonary blood have just returned from the tissues with their hæmoglobin in the reduced state, and the latter at once withdraws oxygen from the plasma. In an instant more oxygen passes out of the pulmonary air into the plasma, from which the oxygen is again quickly withdrawn by the hæmoglobin of the corpuscles, and so on. It is interesting to note that, if the oxygen did not exist in loose chemical combination, it would only be absorbed, and its amount would depend on the barometrical pressure at the moment, and would follow each fluctuation of pressure through a range, say, of one-fourteenth of the total pressure. Such an arrangement could not fail in affecting health. If, on ascending a high mountain, say 15,000 to 20,000 feet above the level of the sea, the pressure sank to nearly one-half, the blood would then contain only half its normal quantity of oxygen, and disturbances in the functions of the body would be inevitable. High-flying birds, soaring in regions of the air where the pressure falls below half an atmosphere, would suffer from want of oxygen; but in deep mines and on high mountains men and animals live in a state of health, and the quick-breathing bird has a sufficient amount of oxygen for its marvellous expenditure of energy, because the amount of oxygen in the blood is independent of the factor which exercises an immediate influence on the gas contents of the fluid—namely, the partial pressure. Kempner has also proved that so soon as the amount of oxygen in the respiratory air sinks only a few per cent. below the normal, the consumption of oxygen by the tissues and the formation of carbonic acid also fall in consequence of the processes of oxidation in the body becoming less active.

It is a remarkable fact that, in certain circumstances, tissues

and even organs may continue their functions with little or no oxygen. Thus, as quoted, Max Marckwald, in his work on the "Innervation of Respiration in the Rabbit" (translated by T. A. Haig, with introduction by Dr. McKendrick; Blackie and Son, 1888): "Kronecker and MacGuire found that the heart of the frog pulsates just as powerfully with blood deprived of its gases as with that containing oxygen, while the blood of asphyxia, or blood containing reduced hæmoglobin, soon stops its action."

Further, Kronecker has found that dogs bear the substitution of two-thirds to even three-fourths of their blood by 0·6 per cent. solution of common salt, and Von Ott withdrew $\frac{14}{15}$ of the blood of a dog, and replaced the same with serum from the horse, free from corpuscles. For the first day or two after the transfusion the dog had only $\frac{1}{55}$ part of the normal number of red blood corpuscles, so that it had only $\frac{1}{55}$ part of its normal amount of oxygen. But this dog showed no symptoms except weakness and somnolency, nor did it suffer from distress of breathing, a remarkable fact when we consider that the blood of an asphyxiated dog still contains 3 per cent. of oxygen, and that it may show great distress of breathing when there is still one-sixth part of the normal amount of oxygen in its blood.

The conditions regulating the exchange of carbonic acid are quite different. We have seen that the carbonic acid is almost exclusively contained in the blood plasma, the smaller part being simply absorbed, and the greater part chemically bound, a portion existing in a fairly firm combination with a sodic carbonate of the plasma, and another portion in a loose, easily decomposable combination with the acid sodium carbonate, and a third portion with the sodium phosphate. Carbonic acid is contained in air only in traces, and its tension in the air is almost nothing. The air contained in the lungs is not wholly expelled by each respiration, but a part of the air of expiration, rich in carbonic acid, always remains in the lung. It is evident, then, that by the mixing of the air of inspiration with the air in the alveoli, the latter will become richer in oxygen and poorer in carbonic acid. The air in the alveoli, however, will always contain more carbonic acid than atmospheric air. Pflüger and Wolffberg have found the amount of carbonic acid in alveolar air to be about 3·5 volumes per cent., therefore its tension will be $\frac{3.5 \times 760}{100} = 27$ mm. of

mercury. The tension of the carbonic acid in the blood of the right ventricle (which may be taken as representing venous pulmonary blood) amounts, according to Strassburg, to 5·4 per cent. = 41 mm. of mercury, and is 14 mm. higher than that in the alveoli. Carbonic acid will, therefore, pass by diffusion from the blood into the alveolar air until the tension of the carbonic acid has become the same in the blood and in alveolar air. Before the state of equilibrium is reached, expiration begins and removes a part of the air out of the alveoli, so that the tension of the carbonic acid again becomes less than that in the blood. During the expiration and the following pause, the elimination of carbonic acid continues. This physical arrangement has the advantage for diffusion, that by expiration the whole air is not driven out of the lungs, for, if expiration had emptied the lungs of air, the diffusion would have ceased altogether during expiration and the following pause, and diffusion have been possible only during inspiration. There would thus have been an incomplete separation of the carbonic acid from the pulmonary blood. But as air remains in the lungs, the stream of diffusion between pulmonary blood and pulmonary air goes on steadily, and fluctuations occur only in regard to its velocity (Munk).

Any account of the gaseous constituents of the blood would be incomplete without a reference to the ingenious theory recently advanced by Prof. Ernst Fleischl von Marxow, of Vienna, and explained and illustrated in his work "Die Bedeutung des Herzschlages für die Athmung; Eine Neue Theorie des Respiration," a work distinguished alike by the power of applying a profound knowledge of physics to physiological problems, and by a keen and subtle dialectic. The author starts with the antagonistic statements that of all animal substances, hæmoglobin is the one which possesses the greatest affinity for oxygen, or that substances exist in the animal body which, at least occasionally, have a greater chemical affinity for oxygen than hæmoglobin possesses. If the tissues have a greater affinity for oxygen than hæmoglobin has, how is it that in the blood of animals that have died of asphyxia there is still a considerable quantity, in some cases as much as 5 volumes per 100 volumes, of oxygen? It is well known that the blood of such animals invariably shows the spectrum of

oxyhæmoglobin. The tissues, then, do not use up all the oxygen of the oxyhæmoglobin, and they cannot, therefore, have a stronger affinity for the oxygen than hæmoglobin has. On the other hand, as the tissues undoubtedly seize hold of the oxygen, and rob the hæmoglobin of it, it would appear as if they really had a stronger affinity for the oxygen. There is thus a contradiction according to Fleischl von Marxow, and it shows that our theories as to the ultimate chemical changes of respiration are not valid.

It might be objected at this point that the death of an animal from asphyxia, while oxygen still remains in its blood, is no proof that the tissues have lost their power of removing oxygen from oxyhæmoglobin. It only indicates that certain tissues, probably those of the nervous centres, require more oxygen than is supplied to them; and, therefore, this part of the bodily mechanism is arrested, with the result of somatic death. Other tissues still live, and use up oxygen so long as their vitality lasts. At the same time, I am willing to admit that it is a striking circumstance that the nervous tissues stop working before they have exhausted every atom of oxygen in the blood.

But if tissues have, as all admit, an affinity for oxygen, and if, at the same time we grant, for the sake of argument, that this affinity is not strong enough to dissociate the oxygen from the oxyhæmoglobin, can we perceive any physical action which would, in the first place, perform the work of dissociation, and then present the oxygen to the tissues in a form in which they would readily take it up? Ernst Fleischl von Marxow holds that he has discovered such an action or agency in the stroke of the heart. He founds his theory on some remarkable experiments, which may be readily repeated with an ordinary tight-fitting hypodermic syringe. (1) Immerse the syringe wholly in water, so as to exclude air. Place one finger over the nozzle, draw up the piston for about half the length of the syringe, and then suddenly remove the finger from the nozzle. The water will rush in, and gas will be given off in considerable amount, the water being quite frothy for a short time. This is what one would expect. (2) Then carefully empty the syringe of air and gently draw it half full of water; then place the finger on the nozzle and draw the piston up a little, so as to leave a vacuum above the water. In these circumstances a few large bubbles of gas will come off, but the water will not froth. (3) Empty the syringe thoroughly, fill it half full of water, raise it obliquely so that the knob at the end of the handle of the piston is above the water, strike the knob sharply with a piece of wood, using the latter as a mallet; then draw the piston up a little, so as to leave a vacuum above the fluid. You will now observe that so large an amount of gas is given off as to cause the fluid to froth. In this experiment, the percussion stroke has evidently altered the mode in which the gas escapes when a vacuum has been formed above it. These experiments may also be done by using a long barometer tube, with a stop-cock at one end, and an india-rubber tube communicating with a movable mercury cistern (a bulb) at the other. By lowering and depressing the bulb, a Torricellian vacuum may be formed, and water may be admitted, as with the syringe. Of the effects of percussion, in these circumstances, there can be no doubt, and the experiments are extremely interesting from the physical point of view. Fleischl von Marxow holds that when gases are dissolved in fluids the condition is analogous to the solution of crystalloids. If a fluid containing gas is shaken, more especially by a sudden sharp stroke, the close connection between the molecules of the fluid and of the gas is rent asunder, and the gas molecules lie outside and between the molecules of fluid. A shock, therefore, converts a real solution into a solution in which the fluid and gaseous molecules are in juxtaposition; and, if a vacuum is formed soon after the stroke, small bubbles of gas make their appearance more readily than if a stroke had not been given.

He then applies this theory to the phenomena of the circulation and of respiration. Starting with the query why the stroke of the heart should be so sudden and violent, when a much slower and more prolonged rhythmic movement would have been sufficient to keep up the tension in the arterial system on which the movement of the fluid depends, he boldly advances the opinion that it serves for the separation of the gases. The blood is kept in motion by a series of quick, sudden strokes, because, for the taking up of the oxygen by the tissues, and the elimination of carbonic acid by the lungs, it is not sufficient that the blood runs steadily through the systemic and pulmonary circulations; and, therefore, a short, hard stroke is given to it immediately before it enters the lungs and immediately after it has left the lungs. These strokes liberate the gases from a state of solution, and they become mixed with the fluid in a state of fine dispersion.

This condition of fine dispersion is favourable for the elimination of the carbonic acid by the lungs, and for the using up of oxygen by the tissues.

Fleischl von Marxow then proceeds to state that loose chemical combinations may also be dissolved by shocks, the gas passing into a condition of fine molecular dispersion, and that a quick repetition of the shocks prevents a recombination. As examples of such loose combinations, he cites oxyhæmoglobin and the compounds of carbonic acid with the salts of the plasma. It is here, in my opinion, that the theory fails, from want of experimental evidence. There is no proof that shocks, such as those of the contraction of the right and left ventricles, can liberate gases from loose chemical combinations such as those with which we have to deal, and it is somewhat strained to point to the explosion of certain compounds excited by strong mechanical shocks or by vibratory impulses.

Some of the applications of the theory are very striking. For example, Fleischl von Marxow suggests that asphyxia occurs before the oxygen has disappeared from the blood, because it is held by the hæmoglobin so firmly that the tissues cannot obtain it. Thus suppose no oxygen is admitted by respiration. It is well known that all the blood in the body passes through the heart and lungs in the time of one complete circulation—that is, in about twenty seconds; and we have it on the authority of Pflüger that in this time one-third of the oxygen is used up by the tissues. According to the percussion theory, the stroke of the left ventricle arterializes the blood—that is, liberates the oxygen from the hæmoglobin—and this arterialized blood is carried to the tissues. The hæmoglobin does not get sufficient time to recombine with the oxygen, because of the successive strokes of the heart and the vibrating thrill kept up in the arterial ramifications. The free oxygen is used up by the tissues in the capillary circulation, to the extent of one-third. After leaving the capillaries, the two-thirds of oxygen again recombine with the hæmoglobin, and in this condition return to the heart, along with one-third of hæmoglobin that has lost its oxygen. In ordinary circumstances this one-third would again obtain oxygen from the alveoli of the lungs; but if all the oxygen there has been used up, of course it cannot obtain any oxygen. The blood flows from the lungs to the left ventricle, when it is again arterialized, and again sent out through the arteries; but as there is now a large amount of free hæmoglobin present in the capillary circulation, it will seize hold of a part of the oxygen, and the tissues will obtain less than the usual supply. With each successive circulation, the amount of oxygen available for the tissues will become less and less, until the tissues receive none, because all the oxygen set free by each beat of the left ventricle is seized hold of in the capillary circulation by the reduced hæmoglobin. The tissues die from want of oxygen, because there is too much reduced hæmoglobin present, a substance having a greater affinity for oxygen than the tissues possess, a result that would probably occur, as in drowning, in the time of six or eight complete circulations—that is, in three or four minutes.

Time will not allow me to refer further to this ingenious theory, which still requires the proof that such shocks as those of the heart can liberate gases from the compounds that exist in the blood. In my opinion, Fleischl von Marxow exaggerates the importance of the shock, while he under-estimates the evidence of the spectroscope, which always shows the spectrum of oxyhæmoglobin even in arterial blood drawn from the neighbourhood of the heart, and kept from contact with the air. Nor can I accept his statement that the force of the stroke of the heart is practically the same in all classes of warm-blooded animals, and one can hardly imagine the feeble stroke of the left ventricle of a mouse would be sufficient to liberate the oxygen from the oxyhæmoglobin of its blood. Further, it may be urged that the conditions of the experiments with the syringe are very unlike those of the circulation, more especially in the fact that the walls of the syringe are rigid, while those of the heart and vessels are yielding and elastic. Again, when an organ is supplied with a solution of oxyhæmoglobin from a pressure bottle, by a process of transfusion, the tissues will reduce the oxyhæmoglobin, and take up the oxygen without any kind of percussion action being brought into play.

Physiologists, however, cannot but treat with the greatest respect the experiments and reasoning of a physicist so able as Fleischl von Marxow is known to be, and the theory will be thoroughly tested in every detail. I may be allowed to contribute an expression of deep interest in this brilliant speculation, and to say that I entirely agree with its author in accepting the suggestions of teleology in the investigations of such problems.

While the rigid investigation of facts is no doubt one of the great methods of science, we must not forget that by asking questions as to the use or value of a particular physiological arrangement, we may obtain light as to the road along which investigations are to be pursued. This is the guiding star of Fleischl von Marxow's speculation, and it has led him and other physiologists to scrutinize anew the theories of respiration now in vogue.

In this address we have had abundant evidence of the fact that physiology, in the solution of some of her problems, depends entirely upon the methods of chemistry and physics. The air-pump, the special advantages of the mercurial air-pump, the methods devised for collecting and analyzing the gases of the blood, the spectroscope, have all contributed important facts to our knowledge of respiration. The narrative placed before you also illustrates in a striking manner the relation of modern physiology to the physiology of our forefathers. The latter were engaged in observing and explaining the more obvious phenomena, whilst the modern physiologists are pushing their researches further, and are endeavouring to study the hidden phenomena, which, like a second order, lie behind these. I need scarcely add that even the results of modern research are not to be regarded as final. Although we see a little further and more clearly than those who went before, there is still uncertainty as to fact and obscurity as to explanation in most departments of physiological science, and not least as regards the function of respiration. Enough has been said to show that in the study of respiratory mechanisms we meet with numerous examples of the same wonderful adaptation of organic structure to physical conditions as may be traced in the mechanism of the eye and of the ear. The structure of a lung or of a gill is just as much adapted for the play of the physical laws regulating gases as the retina is tuned to the vibrations of the ether, or as the organ of Corti responds sympathetically to the waves of musical tone.

List of Experiments in illustration of the Lecture.

1. Appearance of blood after having been shaken with carbonic acid.
2. Appearance of blood after having been shaken with hydrogen.
3. Appearance of blood after having been shaken with nitrogen.
4. Appearance of blood after having been shaken with oxygen.
5. *Fas-simile* model of Leeuwenhoek's syringe, by which gases were first demonstrated in the blood.
6. Absorption of ammonia by water.
7. Gases escaping from water in Torricellian vacuum.
8. Gases escaping from blood in Torricellian vacuum.
9. Spectrum of oxyhæmoglobin shown by electric light.
10. Spectrum of reduced hæmoglobin; the reduction effected by ammonium sulphide.
11. Spectrum of oxyhæmoglobin changing into that of reduced hæmoglobin by heating blood *in vacuo*.
12. Demonstration of a new gas-pump for the physiological lecture table (Figs. 1, 2, and 3).
13. Demonstration of the use of Pflüger's gas-pump.
14. Collection of blood-gases and demonstration of the existence of carbonic acid and of oxygen.
15. Carbonic acid collected from a solution of carbonate of soda *in vacuo*.
16. Method, by use of thermo-electric piles with galvanometer, of observing thermal changes attending formation of oxyhæmoglobin.
17. Demonstration of Fleischl von Marxow's experiments, not with a syringe, but with the fluid in a Torricellian vacuum so arranged as to receive a shock.

Dr. McKendrick asks us to direct the attention of our readers to a statement in his address which he wishes to correct. He stated: "If the union of oxygen with the colouring matter is an example of oxidation, it must be attended with the evolution of heat, but, so far as I know, this has not been measured." He then referred to a method by which Mr. J. T. Bottomley and he had been able to observe the heat produced. Dr. McKendrick was not then aware of an important research on this subject conducted in 1871 by his friend Dr. Arthur Gamgee, and contained in a Report to the British Association for the Advancement of Science in 1871. Dr. Gamgee, both by the use of thermometers and by thermo-electric arrangements, demonstrated the important fact that an evolution of heat accompanies the union of oxygen with hæmoglobin, and in the Report referred to there is ample evidence that the research was conducted with

great skill and with an appreciation of the difficulties to be surmounted. He arrived at the conclusion "that the mean rise of temperature during the absorption of oxygen amounted to $0^{\circ}0976$ C. The maximum heating found was $0^{\circ}111$ C., and the minimum $0^{\circ}083$ C."

MOLECULAR PHYSICS: AN ATTEMPT AT A COMPREHENSIVE DYNAMICAL TREATMENT OF PHYSICAL AND CHEMICAL FORCES.¹

I.

THE author states that his attention was drawn to the subject in the first place by personal intercourse with Sir William Thomson, and by his opening address to the Mathematical and Physical Section of the British Association at the Montreal meeting in 1884, followed by the study of the lithographed report of his lectures on "Molecular Dynamics" at the Johns Hopkins University.

The opening paragraph of the paper contains a restatement of the portions of Thomson's theory applicable to the explanation of optical phenomena. Thomson did not succeed in arriving at a satisfactory explanation of the fact that metallic reflection and double refraction are accompanied by little or no dispersion. The author believes that he has overcome this difficulty by a more complete discussion of the formulæ by expansion in series. He then proceeds to apply the theory to the explanation of chemical phenomena on a purely dynamical basis, and arrives at a method of determining the spectrum of a compound from the spectra of its constituents.

The second portion of the paper is quite independent of the first, and also of Thomson's theories, except that it gives a complete explanation of the manner in which the ether vibrations can be taken up by the molecules of a body.

The author endeavours to explain electrical phenomena by transverse vibrations of the ether, which are very small compared to the diameter of a molecule or of an atom, and one of the most remarkable and interesting results of his investigation is that the theory leads to Weber's law expressing the mutual action of two electric currents, subject to a restriction which excludes exactly those cases the consideration of which led Helmholtz to the conclusion that the law was untenable. A further confirmation of the theory is given by its explanation of a number of other phenomena, such as fluorescence, magnetism, and diamagnetism, and the electro-magnetic rotation of the plane of polarization.

PART I.—LIGHT, HEAT, AND CHEMICAL AFFINITY.

§ 1.—*The Internal Structure of Molecules.*²

The ether is assumed to fill the whole of space, and to be everywhere of equal elasticity and density. It is further assumed that, with respect to vibrations of periods comparable with those of light-waves, the ether behaves like a perfectly elastic solid; while with respect to slower vibrations, such as those due to the motion of gaseous molecules, it behaves like a perfect fluid, so that the molecules can traverse it freely.

A molecule is supposed, on Thomson's³ theory, to consist of a solid core inclosed within a series of spherical shells. Between the core and the innermost shell there is supposed to be an elastic action of a nature which might be represented by a series of symmetrically disposed elastic springs.

A similar elastic action is supposed to take place between every pair of adjacent shells, and also between the outermost shell and the external ether.

Let j be the number of shells in a molecule, and let their masses, beginning with the outermost one, be

$$\frac{M_1}{4\pi^2}, \frac{M_2}{4\pi^2}, \dots, \frac{M_j}{4\pi^2}.$$

The centres of the core and shells may be supposed to lie in a straight line and to be capable of oscillations along this line. The elastic force between each pair of shells is assumed to be proportional to the relative displacement of their centres; and that between the outermost shell and the external ether, proportional

¹ A Paper read before the Physico-Economic Society of Königsberg, by Prof. F. Lindemann, on April 5, 1888.

² The author generally uses the term molecule to denote either an atom or a molecule except when he is considering chemical compounds.—G. W. T.

³ "Lectures on Molecular Dynamics and the Wave Theory of Light," by Sir William Thomson. (Baltimore, 1884.)