THE CROONIAN LECTURES. CONTRIBUTION TO THE HISTORY OF THE RESPIRATION OF MAN.

Delivered before the Royal College of Physicians of London.

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LECTURE I.

MR. PRESIDENT AND GENTLEMEN,—Allow me to begin by returning my best thanks for the honour of being called upon by this College to deliver the Croonian Lectures for the present year. In these four lectures I propose to draw your attention to certain phenomena of human respiration. As far back as 1876 I was led, while mountaineering in the high Alps, to inquire into the influence of altitude on respiration; this work was continued every summer till 1880. The inquiry showed clearly that there was a great deal more to be done on the subject of human respiration; and through the kindness of Professor Schäfer, a laboratory having been placed at my disposal at University College, the work commenced in the high Alps was continued in London, with the aid of assistants, from the year 1883 to the present time.

I propose in this first lecture to treat of the relations of the oxygen breathed with the life of the tissues; the second lecture will be devoted to the various forms of respiration in man; the third to the influence of volition on respiration, and the fourth to respiration carried on under exceptional circumstances, concluding with remarks of a more strictly medical character.

THE VITAL ENERGY AND CHEMICAL ACTION WITHIN THE LIVING BODY.

Vital energy, vital force, or vitality, the cellular life of Virchow, may be defined as power or energy existing in the cell and radiating from it: this cell has oxygen as part of its molecular constitution, and with the aid of this oxygen is constantly undergoing change or metabolism with more or less energy according to age, health, etc.

It might be considered at first sight as if the test of vitality is the degree of power with which life clings to living organisms, such for example as seeds.

Reliable information on this subject is to be found in *Nature Notes* for 1895, where it is stated by Dr. Carruthers that forty years ago Robert Brown succeeded in obtaining the germination of seeds of the *Nelumbium* water lily, which had been preserved in boxes for fifty years in Sir Hans Sloan's collection, and another 100 years in the herbarium of the British Museum. I am much indebted to Dr. Carruthers's kindness in showing me those seeds preserved in acid, which had sprouted to the height of several inches.

Dr. Peter, of Goettingen, has succeeded in obtaining the growth of seeds from the soil of a dense wood with trees 100 or 150 years old; he has also shown that the seeds of many field plants retain their vitality considerably more than half a century. The vital resistance of seeds is moreover illustrated by the fact that they have been exposed to the greatest degree of cold obtainable by artificial means without losing their power of growth. These remarkable phenomena might possibly find an explanation in the following considerations: Life is a contest between vital energy and that other energy known as chemical decomposition. The instant an animal dies chemical decomposition comes into play, and the first change to take place is a combination of the oxygen, which is part and parcel of the molecular tissue. Once that oxygen is gone, recovery of life is impossible.

It has been observed that in the case of animals, one of the first decompositions to set in, has for its result an acid state of the muscles, this acid being looked upon by Catherine Schipiloff from her experiment as the cause of rigor mortis.

If we now return to seed life we shall find that it may be protracted as it were indefinitely under conditions which entirely check decomposition. The seeds of the *Nelumbium speciosum* preserved for 150 years, had dried up and undergone no fermentation, and those cultivated by Dr. Peter had

clearly found in the soil some preserving or sterilising material.

It is but natural to conclude that a molecule of wheat, or of any other seed under such conditions, would retain its oxygen, though without being able to make use of it, because of the absence of moisture, and probably also of certain bacilli which have been found necessary to vegetable growth; hence the seed was not dead, but its life remained in a potential form, or under the form of vibrations too weak to produce any other effect than maintain themselves. So long as oxygen is present as a molecular constituent these vibrations will continue, but they will cease the instant this oxygen has disappeared. It cannot be said that the vitality of seeds is great, but only that seeds under certain atmospheric conditions are not acted upon by those chemical forces known to decompose vegetable tissues. Given an animal suddenly placed in a state resembling death, but in which it could retain its combined oxygen, would it not be possible to maintain its life in abeyance, and ready to be restored on a return to favourable circumstances?

The experiments of Raoul Pictet, the physicist who was the first to liquefy air, appear to give an affirmative reply to this question. In his experiments on fishes he has rapidly frozen them so hard that, according to his statement, they were in a state allowing of their being snapped asunder like a stick, and yet they have recovered life when very gradually thawed. It will be seen in the course of this lecture that when fish are frozen up and completely embedded in the ice during a winter's frost they cannot be brought to life again; hence it appears that the essential condition for the preservation of life is that the fish shall be frozen so rapidly that decomposition cannot possibly commence.

Indeed it is reasonable to conclude that in Pictet's experiments the molecules of tissue were frozen with their oxygen before they had time to dispose of it, and that this oxygen reacting on the molecule of tissue under favourable circumstances brought the fish to life, exactly as it happened that the reaction of oxygen in the seed brought the seed to life after life had been quiescent for fifty or perhaps hundreds of years.

As already stated, no phenomena of metabolism can take place without the interference of oxygen or atmospheric air. The amount of air or of atmospheric pressure required may certainly vary within wide limits, and we all know that with training and slow transition from the seaside to lofty mountain stations a considerable state of adaptation may be obtained. The action of oxygen in the living body, though so far very obscure, is a most interesting study, and first I shall hope to be able to show in a conclusive manner that it is not the oxygen in the atmosphere which by offering itself to the tissues brings about the tissue changes, but because the tissues are undergoing change they require and resort to the oxygen of the atmosphere; hence the more active the change the more oxygen required, and *vice versa*. It is often thought that more carbonic acid is formed when an increased volume of air is voluntarily breathed. This is not so, the excess of carbonic acid given out from the lungs being due to the emission of some of the carbonic acid normally present in the blood, and not to increased combustion, except a very small amount for the extra muscular work of forced breathing.

One of the several objects of oxygen is to produce heat; some of this heat, being transformed into motion, is not perceptible by the thermometer, while another portion manifests itself as heat, and can be directly observed. In cold-blooded animals the heat produced is entirely transformed into motion; this is not the case with warm-blooded animals, which have an excess of heat ready for use; the latter find, therefore, in their bodies a large supply of power wanting in the former.

If the production of heat is so intimately connected with life, that life cannot exist in an active form without it, what is the essential nature of heat? Physicists regard this condition of matter as the result of a vibratory motion of its ultimate molecules, very feeble but very rapid, which is transmitted through the intermolecular and interplanetary spaces by the æther of space. From this view the warmest bodies will be those whose molecules vibrate with the greatest

average death-rate for several consecutive weeks being 9.5 per 1,000 higher than the mean rate for the corresponding periods during the last ten years. It is, of course, impossible to say how far the increased mortality resulted from the long-continued action of the cold on healthy people, but it produced a decidedly lowering effect on persons weak or in ill health.

As stated at the commencement of this lecture, the physical effects of cold on animals have received much attention lately from Raoul Pictet. This gentleman has shown that very low temperatures put an end to all chemical and physical forces. Hydrochloric acid at -130° F. is entirely unattacked by metallic sodium, while at ordinary temperatures they react with explosive violence. In his experiments on animals the temperature of the vessel in which they were placed was gradually lowered from 98.6° to -351° . Pictet concludes from these experiments that warm-blooded animals resist for a considerable time the excessive action of cold, but when their power is on the wane death takes place in a few minutes, the temperature in the centre of the body remaining nearly constant to the end of the struggle for life.

Fishes, frogs, batrachians, and ophidians resist freezing at temperatures varying from 4° to -22° F.; they usually die at a lower temperature. The length of time the animals were exposed to the cold is not stated, and this must be an important factor. Pictet, in one of his lectures, exhibited to his audience a number of gold fish, pike, and frogs frozen, and in the following lecture these same fishes, having been slowly thawed, were shown living and well.

In the *Pall Mall Gazette* for March 23rd, 1891, an apparently authenticated case is quoted of a small fish which had survived six or seven months' enclosure in ice stored in an icehouse at Godalming. I have myself had an opportunity this last winter of observing gold fish which had been caught in the ice. In every case in which the fish was completely embedded in the ice it showed no signs of life on thawing. One of the fish was only partly encased in ice, and had a small quantity of water left round it; when examined it appeared lifeless, but after a time it recovered perfectly. On another similar occasion the fish showed signs of life, but failed to recover. These observations apparently show that, if not absolutely embedded in the ice, the life of fishes can be held in abeyance for a time at a temperature close to freezing, but for how long I cannot tell.

Following up my contention in this first address, these experiments show that the maintenance of the molecular vibration or motion of life requires very little heat in cold-blooded animals, and it may be concluded that at such low temperature as -4° F. the heat is just sufficient to keep up life in the feeblest possible way. If the return of life movements be disturbed by too great an accession of heat, the vibration is immediately arrested, and a most careful handling is required to restore life to its full activity.

At the beginning of this address I remarked as a proposition to be proved that it is not oxygen which by offering itself to the tissues brings about tissue change, but that the tissues make a call—a demand—on the atmospheric oxygen. In favour of this view the influence of cold on vitality was considered, and it was shown that cold up to a certain limit increased the vitality, but beyond that limit produced an opposite effect.

We have now to consider a state of life which to my mind bears some relation to the increased production of carbonic acid in the body from an accession of cold—I mean muscular exercise. The successive phenomena in muscular contraction are as follows: First, volition towards exercise produces an increase in the volume of air breathed, which occurs immediately before contraction or simultaneously with its commencement. At the same time, as will be shown in my third lecture, a certain amount of oxygen is absorbed in the motor centres of the brain corresponding to that muscular exercise. An excess of carbonic acid is now expired, which at first obtains its oxygen from that contained within the muscles, and in proportion as this is used up the oxygen required is taken from the air breathed, the muscles at the same time charging themselves afresh with oxygen from the atmosphere. A number of experiments I made confirm this view. I must also state that we do not know by what process the carbonic acid is formed.

The mode of exercise adopted in my experiment was raising the feet alternately 66 times per minute to a height of about 4 inches, in keeping with the striking of a metronome. The air expired was collected during successive periods and analysed. In the first period of three minutes the oxygen consumed amounted to 719 c.cm. per minute (the second period of three minutes was lost). The third period of three minutes gave 770 c.cm. of oxygen consumed per minute; the fourth, 834 c.cm.; the fifth, 799 c.cm.; and the sixth period of three minutes, 775 c.cm.; this amounting to an exercise of eighteen minutes.

From these figures it will be seen that during the first three minutes of exercise the oxygen consumed was only 719 c.cm. per minute, although the heat required was the same as after six minutes or nine minutes, when much more oxygen was consumed from the air; hence it cannot be doubted that the muscles drew upon their molecular oxygen to a marked extent.

These experiments were made on a former assistant. A series of experiments on myself, and another on my present assistant (Mr. Floris), gave corresponding results.

The connection of exercise with respiration will be more fully inquired into later; in the meantime if, as I contend, the amount of carbonic acid emitted in breathing, or, it might perhaps be more correct to say, the amount of oxygen consumed by the body, is a measure of the vital energy of tissue, then exercise will be a means of keeping up and exciting the life of tissues, and thereby giving them additional power to resist any abnormal change constituting disease. The overdoing of exercise is baneful in a great measure because of the difficulty the body will experience in obtaining from the air sufficient oxygen for the work, but perhaps as much also on account of the trouble required to rid the blood of the excess of carbonic acid formed which accumulates in the circulation.

Muscular exercise is generally looked upon as raising the temperature, although it may also be attended with a cooling effect; and this leads me to consider the question of the body temperature in the act of ascending; but before entering on this subject allow me to offer a few remarks on the methods in use of testing the temperature of the body.

In 1888 I had occasion to enter into a controversy with a Swiss gentleman, Dr. Vernet, who published results he had obtained from taking his temperature while engaged in mountaineering. He maintained that the only correct method of estimating animal heat was by means of a thermometer introduced into the rectum. Being in the habit of taking temperatures under the tongue, a method in general use clinically, I was anxious to ascertain the accuracy of Dr. Vernet's assertion. We accordingly together ascended the Dole, one of the highest points of the Jura, and on nearing the summit, about 4,000 feet in height, we found that with both of us there was a distinct rise of the rectal temperature. This experiment was not, in my opinion, conclusive, as in the act of climbing the blood, from the effect of gravity, must accumulate in the hæmorrhoidal vessels, leading to a state of congestion, and thus to a rise of temperature. The question, however, could only be settled experimentally.

Five simultaneous observations of rectal and sublingual temperatures on different days while resting quiet in bed gave a mean excess of 0.3° F. in favour of the rectal temperature, while very moderate exercise, such as slowly walking about my room, produced a rise of the rectal temperature decidedly in excess of that observed under the tongue. Three experiments gave differences 1.3° , 0.9° , and 0.8° , or a mean difference of 1.0° excess for the rectal temperature, and this was merely from moderate walking exercise in the room, and could not have been due to a general increase of temperature throughout the body; hence it appears that though there may be a very slight increase of the rectal over the sublingual temperature, when taken under circumstances affecting the temperature in both regions equally, still the moment a person is standing or walking the rectal temperature is increased notably beyond the sublingual, which is simply due to a state of congestion produced by gravity.

There remains the possibility of the cold in high altitudes acting through the submaxillary regions, and thus reaching the under surface of the tongue. To clear

up this point I applied pieces of ice under the chin while the bulb of the thermometer was maintained under the tongue. On two occasions there was a perceptible rise in the temperature the moment the ice was applied, a phenomenon also observed by Raoul Pictet in his experiments on the application of cold to animals, and this was followed by a slight fall; the fall in three experiments amounted to 0.2° , 0.6° , and 0.5° in the course of from thirty to forty-eight minutes; therefore the application of ice to the submaxillary region affected but very slightly the sublingual temperature.

The temperature of the body while ascending has been for a long time past subject to discussion. In 1865, Professor Marc Dufour, in his inaugural dissertation to the medical faculty of Zurich, stated from experiments made on himself that in the act of ascending the temperature of the body falls rapidly by about 0.4° F. Another gentleman, Professor Fick, has observed the same phenomenon; many observers find that the body temperature is slightly increased by muscular exercise.

In 1869 I began to give attention to this subject, and invariably found that my temperature fell while ascending; the extent of the cooling being dependent chiefly on the time which had elapsed since the last meal was taken, and to a less extent on altitude and atmospheric temperature. In general the fall of temperature was most rapid when ascending quickly, while fasting and perspiring freely. These inquiries were followed closely by those of Professor Lortet, of Lyons, who obtained similar results.

The observations of Dr. Clifford Allbutt, F.R.S., with three exceptions, gave results opposed to ours.

Many other reliable observations have been published which seem to contradict one another. Thus Professor F. A. Forel, of Lausanne, found that the muscular work of ascending raised the body temperature; Mr. Gay, of Strassburg, observed a decrease of temperature on ascending, and the same phenomenon was observed by Professor Ray Lankester. Hence it must be concluded that the influence of climbing on the temperature of the body varies with different persons. Some in thorough training, young, perspiring but little, and producing as a rule a large amount of carbonic acid, or developing much heat under ordinary circumstances, will observe their temperature to rise in the act of ascending; others, who generally produce less carbonic acid, and therefore develop less heat, will generate just the amount of heat they require for the exercise, but the cold air and perspiration cooling the body, its temperature will fall below the normal.

ON THE RELATION OF RETINITIS ALBUMINURICA TO THE INDUCTION OF PREMATURE LABOUR.¹

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THE subject of this short paper is of interest to the obstetrician as well as to the ophthalmic surgeon, and my object in bringing it under the notice of this Society is to discuss with those engaged in obstetric practice the lines to be pursued in dealing with the class of cases to be mentioned.

Not very infrequently cases present themselves in which it is thought advisable to suggest or sanction the termination of pregnancy, but the question has arisen in my mind, especially recently, not so much as to the correctness of that advice but as to the frequency with which the practice may be resorted to in the same patient. It is a moral as well as a medical question.

Albuminuria is one of the serious complications of the puerperal state, and according to different observers is found prevalent in a percentage of 2 to 6, some giving a less proportion than others. Dr. Parvin² had the urine examined of all the puerperal patients admitted into the Philadelphia Hospital, and found that albumen was not present in more than 6 per cent.

From the obstetric side the importance of the renal com-

plication is, I presume, associated chiefly with the liability of such cases to eclampsia³ and its too frequent bad results. It will, however, hardly be deemed necessary to follow the course suggested by an American oculist "for all physicians to caution mothers to have their daughters' urine examined before they contemplate matrimony."⁴

The seriousness of the renal complication is increased by the sight failure, which is present in a certain number of cases. I have shown elsewhere,⁵ as others have done, that the association of retinitis with Bright's disease is indicative of a very limited period of life, frequently only months. With the albuminuria of pregnancy the retinitis is of less grave import in this respect, but, as far as vision is concerned, it is attended with very serious results. Dr. Culbertson⁶ has collected the cases of albuminuric retinitis which have been recorded, and finds that 23.33 per cent. have terminated in blindness; 58.25 have resulted in only partial recovery of sight, and but 18.54 have recovered sight. Silex,⁷ who has followed 26 patients for a long period, gave the following results: Eleven recovered vision above $\frac{1}{2}$, 10 below this, and 5 were nearly blind, this being due to optic atrophy, choroido-retinitis, and detached retina which showed itself late in two cases.

The retinal affection may show itself at almost any period of pregnancy, and infrequently during the first three months. The appearances in the fundus are generally well pronounced. The margins of the optic discs may be hazy and ill-defined; numerous white patches in the macular region with some hæmorrhages may all be observed. In other cases blindness or great impairment of sight may be present, with an absence of ophthalmoscopic signs. In a case recently which Mr. Richard Favell kindly allowed me to examine, and in which labour was induced for eclampsia at term or nearly so, the young woman was apparently quite blind, but yet there was an absence of ophthalmoscopic signs. On the other hand, the gravity of the retinal affection, as shown by the changes in the fundus, is not always commensurate with the defective vision complained of by the patient, and for this reason it is desirable that pregnant women with albumen in their urine should at intervals undergo ophthalmoscopic examination. It is hardly necessary to enter more fully into this part of the question. The gravity of the complication has been sufficiently dealt with.

Now, it has frequently been found that when labour terminates improvement in sight is apparent, and in this way the induction of abortion came to be advocated. Excellent results have followed its adoption. It has been called for occasionally in my own practice. Mr. R. Favell some time ago undertook in the Jessop Hospital the treatment of such a case for me. But another shortly afterwards, who was to have been similarly treated by Dr. Martin, died in convulsions before arrangements for her removal to the hospital were completed.

The following case is a typical one in many respects:

Mrs. S., aged 21, came first to me at the Sheffield General Infirmary on December 19th, 1893. She complained of her sight having failed for the last six weeks, and in each eye vision was very defective; Left V= $\frac{1}{2}$, Right, barely fingers. In both eyes there was retinitis of an extreme degree. The optic discs were hidden by effusion, and there were numerous white patches and a few hæmorrhages. She had been married twelve months, and was now six months pregnant; there had been no previous pregnancy. She only passed a small quantity of water.

The case was recognised as one of albuminuric retinitis, and of such gravity that if the pregnancy was allowed to continue blindness would most certainly result. My colleague, Dr. Dyson, chanced to be present at the infirmary, and he saw the case with me. We agreed that it was one in which the induction of premature labour was urgently called for, not only on account of the eyesight, but also the danger there was to life in allowing gestation to continue. She had not recently been under treatment, but her medical attendant was Dr. R. M. Clark, of Harthill, and I accordingly wrote giving him the opinion just expressed. I am indebted to his assistant Dr. Baker for the particulars of her case which now follow:

"Mrs. S., aged 21, married at 20 years of age. She suffered from scarlet fever as a child. At the age of 17 she became anæmic, and has remained so ever since. Family history good.

³ "Out of the number of pregnant women suffering from albuminuria about a quarter are attacked by eclampsia.....Death occurs in 30 per cent. of these cases (eclampsia)." (Rosenstein), *Diseases of Kidney*, by Fürbringer, translated by Gilbert, p. 56.

⁴ Culbertson, *Amer. Jour. Ophth.*, 1894, p. 137.

⁵ *Trans. Ophth.*, Vol. viii, p. 144.

⁶ *American Journal of Ophthalmology*, 1894, p. 137.

⁷ *Annales d'Oculistique*, February, 1895.

¹ Read before the North of England Obstetrical and Gynæcological Society at Sheffield, March 15th, 1895.

² *Science and Art of Obstetrics*.