THE LUMLEIAN LECTURES

ON

THE MUSCULAR ARTERIOLES:

THEIR STRUCTURE AND FUNCTION IN HEALTH
AND IN CERTAIN MORBID STATES.*Delivered at the Royal College of Physicians of London.*

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LECTURE I.

The Structure of the Arteries and Arterioles.—The Vaso-Motor Nervous System.—The Physiology of the Circulation.—Influence of the Heart, the Large Elastic Arteries, and the Muscular Arterioles.—The Phenomena of Asphyxia or Apnoea illustrated by Post Mortem Appearances and by Experiments.—Nitrous Oxide Anæsthesia: the Symptoms and their Physiological Explanation.

MR. PRESIDENT AND GENTLEMEN,—In this course of Lumleian Lectures, which, by the favour of yourself, Sir, and the Censors, I am to have the honour to deliver, I propose to discuss certain questions relating to the structure of the minute blood-vessels and the forces concerned in carrying on and regulating the circulation of the blood. Upon this subject modern researches have thrown an entirely new light; and I shall endeavour to show that the increased knowledge of the physiology of the circulation which has been acquired within the last quarter of a century has rendered necessary a revision and correction of some pathological doctrines which had gained more or less general acceptance.

The chief anatomical discovery relating to the organs of circulation made during the period to which I refer was Henle's demonstration of the muscular elements in the middle coat of the arteries. John Hunter and others, it is true, had on theoretical grounds assumed that the middle coat of the arteries contains muscular tissue; but it was Henle (*Wochenschrift für die gesammte Heilkunde*, 1840, No. 21, p. 329) who first described the fusiform muscular elements encircling the arterial tube between the outer and the inner coats, and who showed that these have the same characters as the unstripped muscular tissue of organic life.

There are obvious structural differences, corresponding with important diversities of physiological function, between the large and the small arteries. The chief anatomical distinction between the large and the small arteries is to be found in their middle coat. The middle coat of the largest arteries is composed almost entirely of elastic tissue, with a very slight admixture of muscular fibres. As the arteries diminish in size, the proportion of muscular tissue increases, until, in the smallest arteries, the middle coat is composed entirely of muscular tissue. These smallest arteries are commonly designated "muscular arterioles", to distinguish them from the large elastic arteries. The muscular arterioles, varying in diameter from the one-hundredth to the one-three-thousandth of an inch, have their middle coat composed of muscular fibre-cells, without the slightest admixture of connective or elastic tissue. The muscular fibre-cells, which, when separated, are seen to be elongated and spindle-shaped, with an oblong nucleus in the centre, are arranged in a circular manner round the arteries, forming contractile muscular lamellæ. The circular muscular coat in arteries between about the one-hundredth and the one-three-hundredth of an inch in diameter possesses two or three layers of muscular fibres. In the smaller arteries, the muscular coat consists of only a single layer of fibres, whose elements become shorter and shorter until, in the smallest arteries approaching the capillaries, the muscular elements separate from each other and at length completely disappear.

The muscular coat has on its inner surface the tunica intima, and on its outer the tunica adventitia. The tunica intima consists of two layers: an inner epithelial layer, and a shining membrane which Kölliker calls the *elastic inner coat*. The tunica adventitia consists of connective tissue and fine elastic fibres with elongated nuclei, having their long diameter parallel with the axis of the vessel. The tunica adventitia is generally as thick as, and often thicker than, the muscular coat; and it is readily made to swell up under the influence of certain reagents. My colleague Dr. Beale and other microscopic observers have demonstrated the presence of minute nervous ganglia

and extremely delicate nervous fibres ramifying upon the minute arteries and the capillaries.

During the last quarter of a century, the physiology of the vaso-motor system and the relation between the nervous and the vascular apparatus have been the subject of laborious research by numerous and very able investigators; and the result has been a large addition to our positive knowledge of the forces which are concerned in regulating the movement of the blood through the minutest subdivisions of the vascular system. M. Vulpian, in his two recently published volumes (*Leçons sur l'Appareil Vaso-Moteur*, Paris, 1875), has given a very lucid and complete history of these investigations. An able summary of the physiology of the vaso-motor system appeared in the *British and Foreign Medico-Chirurgical Review* for October 1876; and the whole subject of the vascular mechanism has been treated with great ability by Dr. Michael Foster in his recently published *Handbook of Physiology*.

We have already seen that in the year 1840 Henle had demonstrated the muscular tissue of the middle arterial coat. About the same time, Stilling (*Recherches Pathologiques et Medico-Pratiques sur l'Irritation Spinalé*, Leipzig, 1840) was led to the conclusion that there are certain nerves which influence the movements of the blood-vessels. For these nerves he invented the term *vaso-motor*, and he looked upon them as analogous to the *musculo-motor* nerves. But the starting-point of our present positive knowledge of the vaso-motor nerves was the year 1851, when M. Claude Bernard published his first conclusive experiments (*Comptes Rendus de la Société de Biologie*, 1851, p. 163). In his first memoir, Bernard showed that after division of the cervical sympathetic, but more especially after removal of the superior cervical ganglion, in the horse, the dog, or the rabbit, there is an increased afflux of blood to the ear and the whole of that side of the face, and with this an elevation of temperature and an increased sensibility. In a second communication, made this time to l'Académie des Sciences (*Comptes Rendus de l'Acad. des Sciences*, Mars 29, 1852), he described in more detail the facts recorded in his first paper. It was not until towards the end of the year 1852 that Bernard published his explanation of the phenomena which he had discovered. Meanwhile, public attention having been directed to these researches, in the interval between the publication of Bernard's second and third memoirs, Dr. Brown-Séquard had published in America (*Philadelphia Medical Examiner*, August 1852) the interesting results at which he had arrived. This able experimenter confirmed Bernard's observation of the dilatation of the blood-vessels and the elevation of temperature resulting from division of the cervical sympathetic. He then went on to show that the galvanic stimulus applied to the cut end of the peripheral portion of the nerve caused a constriction of the blood-vessels and a lowering of the temperature. He thus proved that the elevation of temperature resulting from division of the sympathetic is directly due to the increased afflux of blood consequent on paralysis of the arterioles. In Bernard's third memoir, published in November 1852 (*Comptes Rendus de la Société de Biologie*, Nov. 1852, p. 168), he also records the observation that the increased blood-supply which results from the paralyzing influence of dividing the sympathetic is at once arrested by galvanising the divided end of the nerve, when the parts which were previously red and congested become pale and comparatively bloodless.

Since this great field of research was opened up by Claude Bernard and Brown-Séquard, numerous experimenters have laboriously entered upon it, and the result has been the accumulation of many interesting facts and the construction of a tolerably consistent though not as yet an entirely complete theory of the vaso-motor system.

Time would not permit me now, even if it were necessary or desirable, to enter into the minute details of this extensive subject. I need only refer to such ascertained facts and principles as have relation to some pathological phenomena which we shall presently have to discuss. The vaso-motor nerves may be said, in a general way, to belong to the great sympathetic; but, by means of communicating branches, they are also connected with the spinal nerves and with the spinal cord. In fact, there is reason to believe that all the vaso-motor fibres are derived from the cerebro-spinal axis, from which they pass out chiefly by the anterior roots of the spinal nerves; and that the chief centre of vaso-motor nerve action is the medulla oblongata, near the floor of the fourth ventricle. Injury to this part of the nervous centre or division of the cord in the upper cervical region, cutting off the communication between the centre above and the vaso-motor nerves, causes general relaxation of the arterioles and a fall of blood-pressure throughout the body. On the other hand, electrical stimulation of the centre excites general contraction of the arterioles and an increase of blood-pressure.

The nerves which, when divided, cause arterial paralysis, and when stimulated excite arterial contraction, have been designated *vaso-*

constrictor nerves. There are other nerves having a different, and in some respects, an antagonistic function: these are designated *vaso-dilators*. Of this class of nerves, the *chorda tympani* is a conspicuous type.

The *chorda tympani* is a branch of the facial nerve, which joins the lingual branch of the fifth nerve, and is distributed to the tongue and the submaxillary gland. Bernard discovered that electrical stimulation of the peripheral end of the divided nerve causes great dilatation of the blood-vessels of the submaxillary gland, and a rapid and profuse secretion of saliva.

Many experiments of various kinds have proved that the vessels may be made to contract or to dilate by an influence conveyed through incident nerves to the centre, and thence reflected through other fibres to the arterioles. Thus when a sensitive nerve, such as the fifth, or a mixed nerve like the sciatic, has its central end stimulated, a reflex contraction of the arterioles occurs throughout the body, and the blood-pressure rises. On the other hand, Ludwig and Cyon discovered that one branch of the pneumogastric, when its central end is stimulated, has a reflex influence on the vaso-motor nerves, which causes a general relaxation of the arterioles and a consequent fall of the blood-pressure. This nerve, therefore, is called the *depressor nerve*.

There is now a very general agreement amongst physiologists with respect to the influence which the heart, the large elastic arteries, and the muscular arterioles respectively exert upon the circulation. The force which propels the blood through the systemic arteries is derived entirely from the contraction of the muscular walls of the left ventricle of the heart. The elastic walls of the large arteries, distended by the injecting force of the ventricle, contract and force the blood onwards during the diastole of the ventricle. This forcible resiliency in the walls of the arteries is as obviously derived from the muscular contraction of the heart as the elastic power of an archer's bow has its source in the contracting muscles of the arm which bends the bow. The resiliency of the arterial wall, reacting upon the blood during the diastole of the ventricle, gradually converts the interrupted jet of blood from the heart into a continuous current in the minute arteries and capillaries. The muscular arterioles, under the influence of the vaso-motor system of nerves, regulate the blood-supply to the various organs and tissues. The action of the muscular arterioles is, as I have ventured to suggest (*Medico-Chirurgical Transactions*, vol. 51, p. 60), that of stopcocks. By the contraction of the muscular walls, their canals are narrowed, the blood-stream is in a corresponding degree lessened, and the pressure of blood in the larger arteries is increased. On the contrary, relaxation of the walls of the arterioles enlarges their canals, permits a fuller stream of blood to pass, and lowers the blood-pressure in the arterial trunks. The minute muscular arteries, therefore, through their stopcock action, exert a regulating but not a propelling influence upon the blood-current.

The influence of the heart, the larger elastic arteries, and the muscular arterioles respectively upon the circulation, may be demonstrated by the very simple apparatus which I have here.* A pump is made of a hollow India-rubber ball, with two orifices, to one of which is attached a tube six inches long, and to the other an elastic India-rubber tube about four feet long, at the distal end of which is attached a metallic stopcock. The central orifice of each tube is guarded by a bullet valve. The end of the short tube is dipped in a basin of water, while the elastic ball is alternately compressed and relaxed by the hand. The intermitting jet of water from the hollow ball, representing the heart, is gradually converted into a continuous stream by the tube acting thus like the large elastic arteries, and the size of the continuous jet from the metallic orifice is regulated by turning the stopcock. If, now, I substitute for the elastic tube one with rigid walls, the stream of water from the orifice of the stopcock is no longer continuous, but an interrupted pulsating jet; so, if the opening in the stopcock be large enough to allow the water to escape as fast as the pump drives it into the tube, the flow will be interrupted. This wide-open state of the stopcock represents a greatly dilated condition of the muscular arterioles, when the pulse may extend through the capillaries, even into the veins. For the conversion of the intermitting jet from the pump into a continuous stream from the stopcock, it is requisite that the orifice in the latter should be so small as to allow the fluid to accumulate in and distend the elastic tube, the resiliency of which continues to drive on the fluid, while the pump, representing the heart, is dilating to receive a fresh supply.

It is evident then that, while the contraction of the large arteries, which are mainly elastic but partly muscular, aids the heart in propelling the blood onwards towards the capillaries, the contraction of the arterioles, whose middle coat is entirely muscular, antagonises the heart

and the larger arteries; but their stop-action, under the guidance of the nervous system, regulates the blood-supply to the nervous tissues and organs in accordance with their physiological requirements.

There is no evidence of a *peristaltic* muscular contraction of the arteries, as some writers—amongst others, MM. Legros and Onimus—have supposed. Any one who has carefully watched the circulation in the web of the frog's foot, or in other transparent parts of a living animal, must have observed that, so long as the circulation is active, the blood-stream in the terminal arterioles is as continuous and uniform as it is in the capillaries, and there is no appearance of an alternating contraction and relaxation of the arterioles.

The true capillaries have no muscular fibre in their walls, and there is reason to believe that they have no power of active contraction. They become distended and dilated when the muscular arterioles are relaxed, and they return to their original size when the arterioles contract and lessen the blood-stream; but this contraction of the capillaries is probably the result of simple elastic resiliency after distension, and not of an active vital contraction. The capillary obstruction which occurs during the progress of inflammation is of course quite different from a normal physiological impediment.

I now pass on to the consideration of some pathological phenomena which, while on the one hand they receive a more or less complete explanation by the aid of the physiological principles to which I have referred, on the other hand tend to confirm the generally received physiological doctrines relating to the circulation.

The phenomena of what is commonly called *asphyxia*—death, that is, by suffocation or suspension of the respiration—could not be completely and satisfactorily explained before the structure and functions of the muscular arterioles had been revealed. I propose now to devote some time to the consideration of these phenomena, and I shall afterwards endeavour to show that the disturbance of the circulation which results from the suspension of the respiration, is strictly analogous to the hindrances and disorders of the circulation which occur in other morbid states, and especially in connection with certain forms of renal disease.

The immediate cause of death from suffocation is the arrest of the circulation through the lungs. The obvious and indisputable evidence of this is found in the fact that, when the chest is opened immediately after death, the right cavities of the heart and the large branches of the pulmonary artery are found to be greatly distended with blood, while the left cavities are flaccid and comparatively empty. This elementary fact in the pathology of *apnœa* (a term which I use in preference to *asphyxia*, which literally means pulselessness) was first demonstrated by our own illustrious Harvey. Harvey says, "I have several times opened the breast and pericardium of a man within two hours after his execution by hanging, and before the colour had totally left the face, and in presence of many witnesses have demonstrated the right auricle of the heart and the lungs distended with blood—the auricle in particular—of the size of a large man's fist, and so full of blood that it looked as if it would burst. This great distension, however, had disappeared the next day, the body having stiffened and become cold, and the blood having made its way through various channels." (*Second Disquisition on the Circulation of the Blood, Sydenham Society's Translation*, p. 127.)

The great distension of the right cavities of the heart with the relative emptiness of the left cavities, so clearly and accurately described by Harvey, has sometimes been denied by recent writers on *apnœa*, it may, therefore, be well to give some additional evidence of this fundamental anatomical condition.

Dr. Massey of Nottingham, about ten years ago, published the following report of the appearances found in the chest of a man four hours after his execution by hanging (*Lancet*, November 9th, 1867). "On removing the sternum and cartilages of the ribs, the lungs were not to be seen, but were found to occupy a very small space at the back part of the chest, resembling the contents of a foetal thorax, the pericardial sac alone being seen. The colour of the lungs was of a darker hue than natural, especially at the bases. On cutting out the lungs, a quantity of black liquid flowed. The structure was natural, but there was loss of crepitation, and but very little air was contained in them. The right auricle of the heart was gorged at the greatest state of distension with blood, and the inferior cava was in the like condition. On opening the auricle, a great quantity of black fluid blood gushed out. The right ventricle also contained a large amount of blood. The left auricle and ventricle were completely empty."

In October 1867, a dog weighing fourteen pounds and a quarter, was killed in my presence by a ligature on the trachea. The animal continued to struggle convulsively for five minutes. As soon as these movements had ceased the chest was opened. The pericardium was

* This apparatus was designed by Dr. Rutherford (*Lancet*, Oct. 12th, 1872).

so filled and stretched by the distended heart that it was at first supposed that the pericardium had been opened so as to lay bare the heart. The right cavities of the heart were full and tense, the left comparatively empty and flaccid. In particular, the two auricles presented a marked contrast, the right auricle stood out in a globular form and had a tense and elastic feel like an India-rubber ball distended with air, while the left auricle was flaccid and its surface wrinkled. A ligature having been placed round the large vessels, the heart was removed and its cavities opened, when two ounces of blood gushed out of the distended right cavities, while two drachms and a half only flowed slowly from the left side. After division of the large vessels, twelve ounces of blood escaped into the cavity of the chest, chiefly from the *venæ cavæ* and the pulmonary artery. The lungs collapsed to an extreme degree; they were pale and non-crepitant.

It will be seen that the condition of the heart's cavities, and in particular the great distension of the right auricle, as described by Harvey and by Dr. Massey in men executed by hanging, is identical with that which I observed in the dog killed by a ligature on the trachea.

The great distension of the right cavities of the heart, with comparative emptiness of the left, is very generally admitted and believed to result from some impediment to the passage of the blood through the lungs, consequent on the suspension of respiration. The question then arises, What is the mechanism of the process by which the flow of blood through the lungs is impeded and finally arrested? It was formerly supposed that the arrest of the circulation through the lungs might be explained by the cessation of the respiratory movements. It is, of course, indisputable that the movements of the ribs greatly influence the amount of blood within the chest, and especially in the large veins. In inspiration, the blood is sucked into the *venæ cavæ* and the superficial veins in the neck may be seen to collapse; while, in expiration, the intrathoracic trunks are compressed, and the jugulars and other affluent veins are distended; but the hypothesis that the arrest of the blood-stream through the lungs is due mainly to the immobility of the chest is completely disproved by the fact that when an animal is made to breathe nitrogen gas unmixed with oxygen, although the movements of the chest continue as in ordinary respiration, the passage of the blood through the lungs is arrested as speedily and completely as when the chest is motionless. It is evident, then, that the arrest of the pulmonary circulation is in some way caused by the suspension of the chemical changes in the blood and the respired air which are effected by the inhalation of oxygen.

One great step towards the elucidation of this problem was made by Dr. John Reid. He experimented in the following manner upon dogs. A tube with a stopcock was placed in an opening in the trachea, and a mercurial dynamometer was introduced into the femoral artery for the purpose of measuring the blood-pressure within the arterial system. Dr. Reid expected to find that when air was excluded from the lungs by turning the stopcock, and when, consequently, un-aërated black blood began to pass into the systemic arteries, there would be a steady decrease of the blood-pressure there. He found, however, to his great surprise, that for a period of about two minutes after the animal had ceased to struggle, the mercury stood higher in the dynamometer, and the arteries were more tense, than when the animal was breathing freely. After this high pressure had continued for about two minutes, it began to decline rapidly, in consequence of the increasing impediment to the flow of blood through the lungs.

Referring to the temporary increase of pressure in the systemic arteries, Dr. Reid says: "This was so unlooked for, at first sight was so inexplicable and so much at variance with my preconceived notions on the subject, that I was strongly inclined to believe that there must be some source of fallacy; but, after repeating the experiment more than twenty times, and invariably with the same result, I was at last compelled to admit its accuracy. I then began to surmise that this arose from an impediment to the passage of the venous blood through the capillaries of the systemic circulation." We shall presently return to this suggested explanation of the phenomena; meanwhile, it is to be observed that, in experiments performed as Dr. Reid performed his, the observation of the blood-pressure is liable to be more or less interfered with by the struggles of the animal, which, while they continue, have the effect of increasing the arterial pressure.

In some experiments afterwards performed by Mr. Erichsen (*Edinburgh Medical and Surgical Journal*, January 1845), the struggles were prevented by the animal being pithed; and, this disturbing element being thus removed, Mr. Erichsen obtained results which were entirely in accordance with those of Dr. Reid—namely, that with the suspension of the respiration and the consequent passage of black blood into the systemic arteries, there is, for a time, an increased blood-pressure within those arteries, the result of some resistance in the terminal vessels; then, after a period of two or three minutes, there is a rapid de-

crease of pressure, in consequence of the impeded and finally arrested passage of the blood through the lungs.

But the most complete and entirely satisfactory experiments tending to throw light upon the phenomena of apnoea are those which have been performed upon dogs under the paralyzing influence of curara. I am indebted to my friend and former colleague Dr. Rutherford, now the distinguished Professor of the Institutes of Medicine in the University of Edinburgh, for the opportunity of witnessing some experiments performed in 1873, the results of which I will endeavour as briefly as possible to describe. I may state at once that the results, although in some respects more complete and conclusive than those obtained by Dr. John Reid, are entirely in accordance with his observations.

Into the trachea of a dog a tube was introduced and connected with a bellows for the performance of artificial respiration. The voluntary muscles were then paralysed by the injection of curara, and the animal was kept alive by artificial respiration. The sternum and portions of the ribs were removed and the pericardium was opened, so as to expose the whole of the anterior surface of the heart. One common carotid artery was divided, and a dynamometer-tube connected with a kymograph was introduced into the proximal end. In making all these preparations, much time and labour and great skill were required. Artificial respiration was now suspended, and immediately the colour of the left auricle changed from crimson to purple, and the kymograph indicated a continuous increase of pressure in the systemic arteries. After the increase of pressure had continued for about a minute, the left cavities of the heart became much distended; the auricle, in particular, became expanded into a tense globular ball with a smooth surface. In the next period, the pressure in the arteries began to fall, and, about the same time, the right cavities of the heart, which had hitherto remained of the normal size and form, began to expand, while the distension of the left began rapidly to subside. Meanwhile, the right cavities became more and more distended, and now the *right* auricle assumed the appearance of a round tense ball, while the left auricle had become nearly empty and flaccid. The right ventricle also became so distended that it projected above the level of the left.

This was the condition of the heart's cavities when the animal died by the final arrest of the circulation; but, more than once, when the circulation was nearly at a standstill, artificial respiration was resumed, and then all the phenomena rapidly changed. The blood at once passed freely through the lungs, the distension of the right cavities of the heart subsided, and the systemic arterial pressure became first excessive and then normal, when the blood had become thoroughly oxygenised and its passage through the terminal vessels was no longer resisted.

We now return to the consideration of the mechanism of the process by which, first, the systemic and then the pulmonary circulation is impeded when the respiration is suspended.

Dr. Reid maintained that the obstruction occurs in the *capillaries*, in accordance with Dr. Alison's doctrine. He says: "He (Dr. Alison) has shown that this phenomenon is to be referred to an interesting general law of physiology, that has hitherto not received the attention which its importance demands, by which the movement of nutritious juices is influenced by the chemical changes, or, as he terms them, the vital attractions connected with the chemical changes constantly going on in the capillary vessels between those juices and the surrounding tissues by which nutrition and secretion are effected. That such a moving power exists, regulating the movement of the blood that flows through each individual organ, independent of any impulse from the living solids, cannot be doubted. Before arterial blood can be transmitted freely through any tissue or organ, it is not only necessary that the contractions of the heart be performed with a certain amount of force, but that the actions of nutrition and secretion be also in operation; so, in the same manner, before the blood can be transmitted through the lungs, it is not only necessary that the right side of the heart should retain its contractility, but that the chemical changes between the blood and the atmospheric air should proceed. This doctrine is still further illustrated by the fact which we have ascertained, that when the blood in the systemic circulation becomes decidedly venous and unfit for carrying on the process of nutrition, it passes less freely through the capillary arteries into the veins."

In another part of his essay, Dr. Reid expresses his conviction that the irregular afflux of blood to different organs and tissues "cannot be explained by contractile movements of the smaller arteries or capillaries", and he appears to consider that the best explanation of the phenomena has been afforded by Professor Draper, who shows, he says, "in an apparently satisfactory manner how the arterial blood should be drawn into the systemic capillaries, so long as the chemical changes between it and the surrounding tissues proceed, and how the venous blood,

which has no chemical affinities for these tissues, should be driven onwards along the veins to the heart. If this occur in the systemic, the reverse will occur in the pulmonic circulation; for the venous blood has a strong affinity for the oxygen of the atmospheric air that occupies the air-cells upon which the pulmonic capillaries are ramified, while the arterial blood has none, and the venous blood is drawn into these capillaries and drives the arterial blood before it towards the heart."

I have quoted this explanation of the phenomena at some length, because it was the best that could be suggested before the discovery of the structure and functions of the muscular arterioles and of the vaso-motor system of nerves. We are now in a position to substitute for the hypothesis of *vis à fronte*, drawing the blood onwards or retarding its progress, a simple physical explanation of all Dr. Reid's facts, which he himself would have been amongst the first to accept as conclusive. We substitute for mysterious hypothetical attractions and repulsions or suspended attractions, the simple demonstrable phenomena of arterial contraction and relaxation under the influence of nervous agency, and we see how completely this explains the obstruction first in the systemic and then in the pulmonic circulation during the progress of apnoea.

The respiration being suspended, unoxxygenised black blood at first passes freely to the left side of the heart and the systemic arteries and capillaries. Arrived there, either by its direct stimulation of the muscular arterioles or, more probably, by a reflex influence through the vaso-motor nerves and centre, the arterioles are excited to contract, and, by this action of the arterial stopcocks, the blood-pressure in the arterial trunks is increased and the left cavities of the heart become distended and dilated, as seen in the exposed heart of the living dog. The circulation through the systemic arterioles is thus impeded, but not arrested; some black blood passes through the capillaries without undergoing the usual chemical changes, and in this abnormal state it arrives through the veins at the right side of the heart and the pulmonary vessels. Reaching the pulmonary arterioles and capillaries, it excites there the same arterial contraction and resistance as had before occurred in the systemic vessels. The resistance offered by the contracting pulmonary arterioles, while on the one hand it tends to empty the left side of the heart and so to lessen the blood-pressure in the systemic arteries, on the other it causes that great distension and dilatation of the right cavities, more especially of the auricle, which are invariably found to exist when the chest is opened soon after death from apnoea, and which, in Dr. Rutherford's experiment, was plainly seen to occur during the lifetime of the animal.

Some additional facts which were observed during the progress of this experiment are worthy of remark. It was noted that the increased arterial pressure, which commenced as soon as black blood began to pass into the systemic vessels, had existed for some seconds before the left auricle and ventricle began to dilate, and continued for some time after the dilatation of those cavities had reached its height; then, while the distension of these cavities persisted, the arterial pressure began to fall, and it was just at this time that the right cavities, which had heretofore retained their normal size and form, began to be distended and dilated.

The question arises, What was the immediate cause of the diminished arterial pressure which began while the left cavities were still distended? It might possibly be due to diminished contraction of the terminal arteries, but this is not a probable explanation. It was more probably a result of diminished power of the left side of the heart consequent on overdistension of its cavities. It is not unlikely that the heart's contraction may be in some degree enfeebled by the circulation of black blood through its nutrient vessels, but this obviously does not explain the dilatation first of the left cavities and subsequently of the right: a phenomenon which can be accounted for only by excessive contraction, first of the systemic and then of the pulmonary arterioles. We have additional evidence that the weakening of the left side of the heart and the consequent diminution of the arterial pressure, are due to overdistension of the cavities, in the fact that, when, in consequence of the increasing resistance to the circulation through the pulmonary vessels, the blood-supply to the left side of the heart is diminished, the contraction of their muscular walls speedily restores the left cavities to their normal size.

It is manifest from the phenomena which we have been considering—the great distension, first, of the left cavities of the heart, then of the right, and the final rapid arrest of the circulation through the lungs, notwithstanding the forcible contraction of the right ventricle—that the active contraction of the systemic arterioles throughout the body is more than equal to the contractile power of the left ventricle, and the force of contraction in the pulmonary arterioles is more than equivalent to that of the right ventricle.

It is evident that the immediate cause of death from apnoea is the

arrest of the current of blood in the lungs, and this is confirmed and illustrated by the curious fact which was first observed by Buffon, that the young of certain warm-blooded animals—for example, the dog, the cat, and the rabbit—may, within a few days after their birth, be immersed in water of moderate temperature for a period of sometimes half an hour before life is extinct. The explanation of this interesting phenomenon is without doubt to be found in the fact that, in these animals, the foramen ovale and the ductus arteriosus remain patulous for a few days after birth, so that, when, in consequence of the exclusion of air from the lungs, the pulmonary circulation is impeded, the blood passes directly from the right to the left side of the heart and to the aorta, the same as during fetal life, and the circulation consequently continues much longer than in older animals, where, the foramen ovale and the ductus arteriosus being closed, all the blood has to pass through the pulmonary vessels and is thus subjected to their regulating and retarding influence.

With reference to the exact seat of the impediment which arrests the flow of blood through the lungs, I may remark that the extreme anæmia of the minute tissue of the lungs, when examined immediately after death in cases of acute apnoea, is evidence that the stoppage occurs before the blood has reached the capillaries. If, in accordance with the hypothesis of Alison and Reid, the blood were attracted into the capillaries and retained there, in consequence of its not having undergone the normal chemical changes, the capillaries would be in a state of engorgement, and not in that nearly bloodless state in which they are actually found to be.

In the phenomena which attend the inhalation of *nitrous oxide gas*, when given as an anæsthetic, we have a very interesting confirmation of the results obtained by experiments on animals, and, on the other hand, the records of physiological experiments enable us more completely to understand and interpret the facts of nitrous oxide anæsthesia. On several occasions, I have availed myself of the opportunity afforded me by the courtesy of the authorities at the Dental Hospital to watch the phenomena which attend the inhalation of the gas, and I will now briefly describe them.

In most cases, during the first few seconds the pulse and the breathing are quickened, as a result probably of emotional excitement. In the next stage, the breathing becomes slow and shallow and the pulse full and firm. Then, after a period which varies in different cases from forty to eighty or ninety seconds, the pulse suddenly becomes almost, or even quite imperceptible, the features become livid, the pupils are widely dilated, there is a state of general muscular rigidity; in short, all the phenomena of the first stage of an epileptic fit are present. The mouth-piece being removed, the morbid phenomena quickly pass away, the features regain their normal colour, the pulse returns, and for a few seconds has again a full and throbbing character, but quickly regains its normal condition.

The explanation of the phenomena appears to be sufficiently obvious. It is admitted on all hands that, at the temperature of the body, the nitrous oxide gives up no oxygen to the blood or the tissues. The gas becoming rapidly diffused and replacing the oxygen in the lungs and in the blood, black unoxxygenised blood passes into the systemic arteries, and excites, through the vaso-motor nerves and centre, contraction of the muscular arterioles. The resistance thus offered to the passage of unœrated blood through the terminal arteries explains the temporary fulness and tension of the radial pulse. The unoxxygenised blood, passing through the systemic capillaries without the usual interchange of materials between it and the tissues, returns to the lungs in an abnormal condition, and there excites contraction of the pulmonary muscular arterioles. The resistance thus offered to the passage of blood through the lungs explains, on the one side, the systemic arterial emptiness with feebleness or even complete disappearance of the pulse, and, on the other, the systemic venous fulness with lividity of the skin. The epileptiform condition is explained by the sudden and extreme diminution of the blood-supply to the brain, the blood at the same time being unœrated.

If the inhalation were continued, death would occur from the complete arrest of the pulmonary circulation and consequent overdistension of the right side of the heart, and this is the mode in which death occurs when an animal is killed by the continued inhalation of the gas. A year ago, my friend and colleague Mr. Hamilton Cartwright assisted me to kill two rabbits with the gas. In both animals, convulsions preceded death; and, the chest being opened immediately after death, the heart was found still beating. The right cavities and the systemic veins were greatly distended with blood, while the left cavities and the aorta were comparatively empty and flaccid; the blood on both sides of the heart being equally black. The lungs were anæmic and collapsed to an extreme degree.

It will be seen that the phenomena observed during life and the appearances after death from the inhalation of the nitrous oxide gas are precisely similar to those which result from suspension of the respiration in the human being and in the lower animals.

It is evident, from the many thousands of cases in which the gas has been given and the extreme rarity of a fatal accident from its use, that, in the hands of a skilled and careful operator, no great risk attends the employment of this anæsthetic; but it is also obvious that, to a patient with a feeble fat heart, the distension of the right cavities which accompanies the disappearance of the radial pulse and the general lividity of the features must be attended with some degree of risk, and the danger must be increased when, the muscles of the trunk and limbs being convulsed, the pressure of the contracting muscles upon the veins drives the blood forcibly towards the right cavities of the heart, and so adds to their distension.

THE CROONIAN LECTURES

ON

THE DIFFERENCE BETWEEN THE SEXES IN REGARD TO THE ASPECT AND TREATMENT OF DISEASE.

Delivered at the Royal College of Physicians of London.

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LECTURE III.

I OCCUPIED the last lecture in discussing those complaints which seemed to depend chiefly on disturbances of the ganglionic system, directly or indirectly. There is one other disease which seems to be dependent on a similar state. I mean

Exophthalmic Goitre, or Graves's Disease.—In some kind of mutual relationship with the conditions we last considered, we find other diseases, regarding which, recent observations have led to the belief that they arise from disturbances of the sympathetic nerves. And here we find, as we have already done, where the sympathetic is troubled, that women are more prone to its disturbances.

Now, in exophthalmic goitre or Graves's disease, we find, as you are already aware, that females are affected largely in excess of males. Accompanied, as it is very commonly, with anæmia and disturbances of the menstrual function, we can recognise in it a depression and perhaps irritation of the sympathetic system. Maunsell mentions that, out of fifty cases, forty-two were females.

But it is not only in exophthalmic goitre that the excess is so much on the side of females. In simple *bronchocele* we find the same, and also in the other forms occurring chiefly in the young and during pregnancy; while compound bronchocele was met with in one hundred and five females to fifteen males out of one hundred and twenty cases.

I have thus very briefly touched upon the affections in which the sympathetic or ganglionic system is affected. We must now consider those in which the cerebro-spinal system is principally involved.

I have already shown the great frequency of *Talipes equinus* among male new-born infants. I have alluded to the greater number of deaths of male infants, and to the fact that congenital idiocy is most prevalent in first-born males. With regard to *insanity*, the difference between the sexes in number is not very marked. But the relative frequency in the sexes varies in different countries. In the tables given by Dr. Jarvis (*Comparative Liability of Males and Females to Insanity, etc.* Utica, 1850), we find that males predominate in the asylums of America, England, Scotland, Ireland, and France; females in those of Belgium, Norway, Paris, and the pauper classes of England and Wales. In Naples, there were two females to one male; while in Milan this proportion was reversed.

As to the causes of this difference in the two sexes, I cannot do better than quote his words: "In as far as men, from their habits, their position, and their exposures, are more frequently intemperate; in so far as they have more of the sexual passion and less delicacy of sensibility, and are therefore more given to masturbation and sensuality; in as far as they are more involved in business, more interested in property and in politics, in schemes of aggrandisement and in pursuit of knowledge, and are therefore more frequently bankrupt, or disappointed, or overwrought with labour and anxiety; in as far as they are employed with machinery, and with powder, or more frequently travel

and go over dangerous places, or are involved in strife and bodily quarrels, and therefore meet with accidents, falls, blows on the head, etc., than women, there are more male than female lunatics. But, in as far as females have more sensibility and stronger affections, and more active sympathies, and therefore suffer more intensely from grief, and loss, and sickness of friends, and more from a cause almost peculiar to themselves, in the want of domestic sympathy, and in the ill-treatment of intemperate and unkind husbands or children, or other kindred; in as far as females are more sedentary, and are therefore more frequently dyspeptic, or suffer secondary irritation from the sympathy with the reproductive system, and therefore more ill-health; and inasmuch as they are more timid, and are therefore more exposed to fright—females are more liable to insanity than males."

Dr. Meyer of Berlin shows how deeply the sympathetic system is involved in the disturbance, if we may consider that menstrual anomalies are indication of such. Out of 6,000 insane women and girls, there were 1,138 or 18.97 per cent. without, while there were 4,862 or 81.03 per cent. with, menstrual derangements. The excess of menstrual disturbances was more notable in the better class than in the poor, in the proportion of 94.87 per cent. in the former to 67.02 per cent. in the latter.

It would be difficult to estimate how far functional irregularities acted directly or indirectly, or how far the mental disturbance produced effect directly on the functions, or indirectly by interference with appetite, digestion, or exposure, etc. In either case, no doubt, there is a general tendency in the majority to derangements both of cerebro-spinal and ganglionic systems, and each plays to a variable but appreciable extent, in the several cases, into the hands of the other.

The *diseases of the brain*, except those I have mentioned, occur very nearly equally in the two sexes. One disease, epilepsy, in which one would have expected an excess on the side of the females, because it is most frequent at and about the period of puberty, is equally frequent in both sexes. But, as is well known, woman in the pregnant state is exposed, not rarely, to attacks of *eclampsia*. How far this bears any relation to epileptiform convulsions in the male, it is difficult to say. It was, in the pregnant female, formerly supposed to be owing to the uræmic state; but it has not so simple a pathology, as this uræmia does not previously exist in many cases. Vascular excitement and tension have something to do with it; and the reflex irritation of the pregnant uterus, and often of the intestinal canal, must be taken into account amongst the probable factors.

In investigating this matter, I found that the urine, passed just before the convulsion, in half the cases in which I could secure it, had no albumen, though all subsequently had it. I think it is not unlikely that this may be found in some of the supposed uræmic convulsions in the male; for Dr. Moxon saw a case of a lad who had violent convulsions, and the first urine was free from albumen, but shortly afterwards it was found in considerable quantity. But I must not detain you longer on this, to obstetricians, interesting and important condition.

The *diseases of the spinal cord* are much more frequent in the male. Thus, in Dr. Brown-Séquard's 177 cases of all kinds of spinal disease, 128 occurred in males and only 49 in females. In locomotor ataxy, this is strongly pronounced. But there is one condition, on which I wish to make a few remarks, that finds its victims among females. This has been called *spinal irritation*, and has been classified as a distinct disorder. Without attempting to decide whether sometimes there is a primary centric cause, I would wish to record the opinion, derived from long and careful attention to the subject, that in the majority of cases there is an eccentric origin, and that principally of the internal organs, which by their disorder cause a reflex irritation on a corresponding part of the spinal cord, and then an extension to the nerves which pass out behind; sometimes only to those supplying the surface over the vertebrae; sometimes extending to those which pass to the front, when it has the form of neuralgia more clearly marked. I take it that it exactly corresponds to the sacral pain in women in labour or suffering from uterine disorders.

This pain, besides the aching over the sacrum, as I have before shown, is accompanied by a distinct tenderness of the skin, limited to a space generally of two or three inches in diameter, most commonly in the centre, sometimes on one side. When touched it is tender, sore, and is relieved by anodynes; in other words, the nerves of the skin are reflexly sensitive and in a state of irritation. Pressure, as is well known, benumbs it; and nothing shows its origin better than its complete subsidence on the cure of the internal cause; though, in long-standing cases, it is some time before all this effect has passed off, and a slight return of the cause will more quickly set up pain than at first; from which fact, I think we shall be right in assuming that the part of the spinal cord in connection with the disorder becomes itself affected in some manner;