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 / by George Johnson.

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.

BY

GEORGE JOHNSON, M.D., F.R.S.,

FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS; PROFESSOR OF CLINICAL MEDICINE AND SENIOR PHYSICIAN TO KING'S COLLEGE HOSPITAL, ETC.

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THE MUSCULAR ARTERIOLES: THEIR STRUCTURE AND FUNCTION IN HEALTH AND IN CERTAIN MORBID STATES.

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 Apnœa 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 unstriped 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 vasomotor 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 Spinale*, 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 paralysing 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 mus-

cular 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

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

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 fœtal 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 crepitancy, 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 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, unaërated 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 decrease 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 apnœa are those which have been performed upon dogs under the paralysing 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 vasomotor 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 apnœa.

The respiration being suspended, unoxygenised 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 apnœa, 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 apnœa 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 fœtal life, and the circulation consequently continues much longer than in older animals, where, the fora-

men 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 apnœa, 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 unoxygenised 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 unaërated blood through the terminal arteries explains the temporary fulness and tension of the radial pulse. The unoxygenised 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 unaërated.

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.

Lecture II.

The Relation between Renal Disease and Hypertrophy of the Heart.—Various Hypotheses.—Hypertrophy of the Muscular Arterioles: its Relation to Renal Disease and to Cardiac Hypertrophy.—Results of Arterial Tension in Bright's Disease. 1. *Degeneration of Arterial Walls.* 2. *Cerebral Hæmorrhage.* 3. *Reduplication of the First Sound of the Heart: its Cause and its Practical Significance.*

I PROPOSE now to discuss the state of the circulation in cases of Bright's disease, and the influence of the muscular arterioles in the causation of the phenomena.

Dr. Bright was the first to point out the frequent association of disease of the kidney with disease of the heart. In a paper published in the first volume of the *Guy's Hospital Reports*, while passing under review the chief morbid appearances observed in one hundred cases of renal disease connected with albuminous urine, he refers to the subject of cardiac disease in the following terms. "The deviations from health in the heart are well worthy of observation; they have been so frequent as to show a most important and intimate connection with the disease of which we are treating; while at the same time there have been twenty-seven cases in which no disease could be detected, and six others which, from not having been noted, lead to the belief that no important deviation from the normal state existed. The obvious structural changes in the heart have consisted chiefly of hypertrophy, with or without valvular disease; and, what is most striking, out of fifty-two cases of hypertrophy, no valvular disease whatsoever could be detected in thirty-four, but in eleven of these thirty-four more or less disease existed in the coats of the aorta; still, however, leaving twenty-three without any probable organic cause for the marked hypertrophy generally affecting the left ventricle. This naturally leads us to look for some less local cause for the unusual efforts to which the heart has been impelled; and the two most ready solutions appear to be, either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately, or that it so affects the minute and capillary circulation as to render greater action necessary

to force the blood through the distant subdivisions of the vascular system."

Now, the problem to be solved is the relation between disease of the kidney and hypertrophy of the left ventricle, when there exists no disease of the valves or of the large arteries to account for the hypertrophy. This subject has been much discussed of late; and, although I have nothing absolutely new to bring forward on the present occasion, I shall endeavour so to arrange the facts and arguments which bear upon the question as to assist in the formation of a definite opinion with regard to some hitherto debated points.

It is generally admitted that the hypertrophy of the left ventricle in the cases under consideration is the result of some impediment in the course of the circulation, to overcome or counterbalance which the heart has been impelled to unusual efforts; and, when the arterial trunks and the larger branches are in a normal state, it is evident that the impediment must exist somewhere beyond, in what Dr. Bright calls the "distant subdivisions of the vascular system".

One hypothesis may be mentioned and dismissed in a few words as being utterly inadequate. I allude to the suggestion of Traube (*Ueber den Zusammenhang von Herz und Nierenkrankheiten*, Berlin, 1856), that, when the kidney is in an advanced stage of atrophic degeneration, a diminished quantity of blood passes through it; there is, therefore, increased tension of the renal artery and aorta, and consequently more forcible contraction of the left ventricle, with resulting hypertrophy. This explanation is obviously insufficient. The diminished circulation through the kidney alone, even in the most advanced stage of granular degeneration, would not give rise to the great amount of hypertrophy of the left ventricle which is commonly found in these cases; nor would it cause the high arterial tension throughout the system which is associated with the cardiac hypertrophy.

I believe that one step towards a solution of this problem was made by myself more than a quarter of a century ago, when, in a paper communicated to the Royal Medical and Chirurgical Society and published in the thirty-third volume of the *Transactions*, I described for the first time the remarkable hypertrophy of the muscular walls of the minute renal arteries in the advanced stages of chronic Bright's disease. In that paper, I correctly described and represented in drawings the hypertrophy of the arterial walls; but my physiology was at fault, and I wrongly interpreted the phenomena. The paper in question was read and published in the year 1850—a year, that is, before

the publication of Bernard's first memoir describing the results of his experiments on the vaso-motor nerves. At that time, it was very generally supposed—at any rate, I had been taught to believe—that the contraction of the muscular arterioles assists the heart to propel the blood onwards through the capillaries; and, in accordance with that belief, I endeavoured to explain the arterial hypertrophy by the increased muscular contraction required to overcome the impediment resulting from the destruction of the glandular tissue and the inter-tubular capillaries. The researches of Bernard and Brown-Séquard referred to in my first lecture, resulting as they did in demonstrating that the function of the muscular arterioles is to regulate the blood-stream, and not by their contraction to assist in driving the blood onwards, convinced me that my explanation of the hypertrophy of the renal arteries was untenable; but several years elapsed before I ventured upon any other explanation of the facts. Meanwhile, having daily opportunities of confirming Dr. Bright's observation of the very frequent coexistence of chronic renal disease with cardiac hypertrophy —observing, too, the clinical fact, readily ascertained by the finger and confirmed by sphygmographic observation, of high arterial tension in this class of cases—it occurred to me, thoroughly imbued as I had become with the vaso-motor doctrines of Bernard and Brown-Séquard, that we must look to the influence of the muscular arterioles, and what I have ventured to call their stopcock action, for the explanation of that peripheral impediment to the circulation which results in the arterial tension and the cardiac hypertrophy of Bright's disease.

The course of the argument was this. It is an established physiological doctrine, that the contraction of the muscular arterioles diminishes the blood-stream, calls forth more forcible contractions of the left ventricle, and so increases the blood-pressure in the arterial trunks. It is a physiological law, that increased muscular contraction leads, within certain limits, to increased growth—hypertrophy—of muscular tissue; and this is especially true of the involuntary muscles. If, therefore, in the course of chronic Bright's disease, the morbid quality of blood excites such forcible and long continued contraction of the muscular arterioles, and thereby so increases the work of the left ventricle as to cause great hypertrophy of its walls, it is probable that the muscular walls of the arterioles will be found to have become simultaneously and in a corresponding degree hypertrophied. The next step was to make a microscopic search for the arterial hypertrophy in other tissues than the kidney, where I had discovered and

described it years before; and the result was, that the arterioles in various tissues, more especially in the subcutaneous and the submucous tissues, in the muscles, and in the pia mater of the brain, were found to have their muscular walls thickened by a true hypertrophy—by an increase, that is, of their muscular tissue, without structural change or degeneration. The general results of these observations are recorded in a paper which was published nine years ago in the fifty-first volume of the *Medico-Chirurgical Transactions*. I have the satisfaction of knowing that the publication of that paper has had the effect of directing the attention of many competent observers to the condition of the minute blood-vessels in connection with Bright's disease; and, although some of my statements and conclusions have been disputed, I believe that, in the main, my record of facts and my inferences will be found to bear the test of time and criticism.

Some writers have gone so far as to deny the existence and even the possibility of hypertrophy of the muscular coat of the arterioles; but, on the other hand, very competent observers have confirmed my observation of this change in the arterial walls. Amongst these, some have asserted very strenuously that not only is the muscular coat thickened, but the other coats also. I have never denied this, but, on the contrary, I have looked upon it as a matter of course. Just as in the hypertrophied left ventricle there is an increased growth not only of the muscular fibres, but also of the connective and other tissues which constitute the walls of the ventricle, so in a hypertrophied arteriole there is a duly proportioned increase of the outer and inner as well as of the middle muscular coat.

We have now to inquire what are the conditions in which this arterial hypertrophy occurs. What is the physiological explanation of its occurrence? And what are the results of this arterial change?

The associated renal and cardiac hypertrophy are found to occur in the last stages of all the forms of chronic Bright's disease—most constantly and conspicuously in cases of the small red granular kidney; but very frequently, too, as the observations of Dr. Grainger Stewart, Dr. Dickinson, and others, have shown, they are found to occur with the large white kidney which has passed on to the stage of more or less advanced granular contraction. My own observations have led me to the conclusion that there is a direct relation between the destruction of the renal gland-cells and the cardio-arterial hypertrophy; and I will presently suggest an explanation of this relationship.

I must here once more insist upon the fact that the primary and essential

structural changes in the small red granular kidney are not interstitial, as the term "interstitial nephritis" implies, but glandular. There is no form of Bright's disease in which the gland-cells are so constantly and extensively destroyed as they are in this. The microscopic evidence of the destruction of the renal cells is to be found during life in the numerous granular casts, composed of disintegrated renal epithelium, which appear in the urine, and after death in the more or less general appearance of transparent tubes denuded of their epithelium and in various stages of atrophy or dilatation.

The *clinical evidence* of the destruction of the essential secreting tissues in this form of disease is afforded by the notorious fact that symptoms of uræmic poisoning—poisoning, that is, from the retention within the system of various kinds and combinations of urinary excreta —are more common in this than in any other variety of Bright's disease.

On the other hand, in the cases of chronic Bright's disease associated with a large white kidney, the enlargement of the organ up to a certain point is mainly the result of a kind of hypertrophy of the glandular tissue, and with this there may be little or no evidence of uræmia, of arterial tension, or of cardio-vascular hypertrophy. But when the renal disease passes on to the stage of atrophy, with coarsely granular contraction of the cortical portion of the gland, uræmia and resulting structural changes in the heart and arteries are commonly found to be associated therewith.

There is yet another class of cases which have an important bearing upon the question of the relationship between renal disease and the associated cardio-vascular changes: I mean cases of acute Bright's disease. In 1873, Dr. Galabin published a pamphlet *On the Connection of Bright's Disease with Changes in the Vascular System*, in which he showed, by the evidence of sphygmographic tracings, that, "even in the early stages of acute nephritis, such an impediment to the circulation may occur from altered quality of the blood, that the arterial pressure is increased and the heart's contraction made more laborious"; and he added, "if this be true, it is easy to understand that this state of things, if continued long enough, will cause the muscular walls, both of heart and arteries, to hypertrophy". And our late lamented friend and colleague Dr. Sibson, in the Lumleian Lectures (*Lancet*, March 28th and April 4th, 1874), which he delivered here three years ago, and in two Harveian Lectures (BRITISH MEDICAL JOURNAL, January 6th and 13th, and February 10th and 24th), given last year, showed, by a series of elaborate and careful observations, that, in cases of acute Bright's disease,

there may occur, as a temporary and transient condition, increase of arterial tension, felt by the finger and demonstrated by the sphygmograph, distension and incipient hypertrophy of the left ventricle, doubling of the first sound of the heart, and an intensified metallic second sound over the aorta: these modifications of the normal cardiac sounds being results and indications of high arterial tension.

The observations of Drs. Galabin and Sibson are entirely in accordance with my own daily experience, and they have been confirmed by many other physicians. What, then, is the explanation of the systemic arterial tension of acute Bright's disease? Without doubt, it is a result of uræmic poisoning; and I believe it to be precisely analogous to the arterial tension, with distension and dilatation of the left cavities of the heart, which have been demonstrated to occur in the early stages of apnœa, when, as I endeavoured to show in my last lecture, the passage of unaerated black blood into the systemic arteries excites, through the vaso-motor nerves and centre, contraction of the muscular arterioles, and thus causes distension of the arterial trunks and of the heart's cavities. We have additional evidence of the close analogy between the uræmic and the apnœal conditions in the fact that, amongst the results of advanced emphysema of the lungs with chronic bronchitis and the consequent passage of imperfectly oxygenised blood into the systemic arteries, we find, not uncommonly, a full, tense radial artery, and after death more or less considerable hypertrophy of the left ventricle. In one case of emphysema with chronic bronchitis and hypertrophy of the left ventricle, the subcutaneous arterioles, of which I have a preserved specimen, are very decidedly hypertrophied.

Obviously, then, there are striking analogies between the phenomena of uræmic poisoning and those which attend the passage of unaërated blood into the systemic arteries.

Before I pass on, it may be well to refer briefly to two suggested explanations of the impeded circulation in Bright's disease different from that which I have here given.

One theory is, that the thickening of the vessels which I describe as hypertrophy of the muscular coat, is not hypertrophy at all, but a degeneration of the coats of the arteries. This question is one of microscopic observation, and can be decided only by an appeal to the anatomical facts. But I may remark, in passing, that degeneration of the muscular arterioles would not explain the phenomena. Since it is certain that the contraction of the muscular arterioles exerts an influence which, by limiting and retarding the blood-stream, antagonises the heart, it is

obvious that degeneration of their muscular walls would involve, not an increase, but a decrease of resistance; and so, on this hypothesis, the increased arterial tension and the cardiac hypertrophy are inexplicable. It is evident, too, that degeneration of the arterial walls would not explain the rapid onset and the passing away again of the high arterial tension in cases of acute Bright's disease.

The other hypothesis to which I just now referred is that which attributes the impeded circulation in cases of Bright's disease, not to the contraction of the muscular arterioles, but to "an impediment in the capillaries, due to a modification of capillary attraction between the blood and the walls of the vessels; and, the arterial pressure being thus increased, the muscular walls of heart and arteries are both hypertrophied in concert, since both have to act against greater resistance" (Dr. Galabin, *op. cit.*, p. 10). The obvious objection to this hypothesis is, that an imaginary "capillary force" is substituted for the demonstrated physiological function of the muscular arterioles. There was a time when the theory of a capillary force served the useful purpose of linking together a number of facts regarding the circulation through the terminal vessels; but Henle's demonstration of the muscularity of the arterioles, and the physiological discoveries of Bernard and Brown-Séquard, have rendered that hypothesis as untenable as the theory of phlogiston was made by the discovery of oxygen gas.

The substitution of an imaginary subtle capillary attraction for the obviously adequate influence of the muscular arterioles, reminds one of the curious hypothesis by which Riolanus, in opposition to Harvey, endeavoured to explain the passage of the blood from the right to the left side of the heart. Harvey, referring to this, says—"He (Riolanus) would have the blood to make its way into the left ventricle through the septum of the heart by certain invisible and unknown passages, rather than through those ample and abundantly pervious channels the pulmonary vessels, furnished with valves opposing all reflux or regurgitation" (Harvey's *Works*, Sydenham Society's Translation, page 99).

Even if there existed in the capillaries a power of arresting the passage of the blood, mere passive distension of the arterioles, in consequence of an obstruction in front, would not result in hypertrophy of their walls. This is proved by specimens showing no thickening of the arterioles, in the lung of a patient who had chronic incompetence of both the mitral and aortic valves, with much pulmonary engorgement and hæmoptysis.

That a persistent active contraction of the muscular arterioles is the cause of the impeded circulation and of the resulting arterial tension in cases of chronic renal disease, seems to be proved almost to demonstration by the remarkable hypertrophy of the arterial walls; and this view receives confirmation from the influence of nitrite of amyl in lessening the arterial tension. This agent, when inhaled, has the power of causing rapid and extreme relaxation of the arterioles, and consequent injection of the capillaries; and Dr. Broadbent was the first to show that, in a case of contracted kidney, with high arterial tension, the blood-pressure was much lessened by the inhalation of nitrite of amyl. Dr. Sibson repeated this experiment with the same result. He says, "under the influence of the amyl, there was less tension; and, as the tension was removed, the doubling of the first sound was lost".

It is obvious that the nitrite of amyl could not thus influence arterioles rendered rigid by degeneration of their muscular tissue.

An interesting confirmation of the theory that contraction of the muscular arterioles is the cause of the increased arterial tension is afforded by some ophthalmoscopic observations lately recorded by Dr. Gowers (BRITISH MEDICAL JOURNAL, Dec. 9th, 1876, p. 743). In five successive cases of Bright's disease, in different stages and with different degrees of arterial tension, Dr. Gowers observed a direct relation between the contraction of the magnified terminal arteries in the retina and the degree of arterial tension at the wrist. And he argues that, "as the immediate effect of contraction of the arterioles must be an increase in the arterial blood-pressure, it is reasonable to conclude that such is the sequence of events in the phenomena under consideration, that, although the two phenomena may be in part the result of a common cause (altered state of the blood), the contraction of the arteries seen in those of the retina, and inferred to exist elsewhere, is, in part at least, the cause of the increased blood-tension".

And now, having, as I believe, adduced sufficient evidence to show that the arterial tension in Bright's disease is a result of the resistance to the blood-stream caused by the contraction of the muscular arterioles, this undue contraction being excited by the influence of contaminated blood upon the vaso-motor nervous system, I pass on to the consideration of some of the *results* of the increased blood-pressure and arterial tension.

I have already referred to the hypertrophy of the left ventricle as an intelligible physiological result of the more forcible muscular effort

required to propel the blood through the resisting arterioles. During the progress of the cardio-vascular changes, it happens not unfrequently that the walls of the large arteries undergo more or less of structural change. They become thickened and indurated, and, as a result of these textural changes, their elasticity is more or less impaired. These structural changes in the walls of the larger arteries may be partly caused by the excessive strain to which they are subjected under the influence of the high tension resulting from the antagonism between the resisting arterioles and the hypertrophied ventricle. It is a matter of common observation, that the walls of the arch of the aorta not unfrequently have their texture injured and their elasticity impaired by the forcible distension to which they are subjected when, in consequence of incompetence of the aortic valves, the left ventricle has become much dilated and hypertrophied.

In part, perhaps, the arterial degeneration in cases of Bright's disease may be excited by the morbid quality of the blood which they are continually transmitting — the same morbid quality of blood as that which not uncommonly sets up inflammatory changes in the lining or the investing membrane of the heart itself. Whatever may be the determining cause of the structural changes in the larger arteries, it is certain that, since the elasticity of the large arteries is a force which aids the heart in propelling the blood onwards, the loss or impairment of that elasticity must add to the work of the heart, and thus tend to increase the hypertrophy of the left ventricle. Hence the resistance to the blood-current resulting from the excessive contraction of the muscular arterioles is still further increased by the not infrequent complication of degeneration of the walls of the large arteries.

Dr. Galabin, in the pamphlet before referred to, has shown, from a comparison of the *post mortem* records at Guy's Hospital, that hypertrophy of the left ventricle is more frequently associated with granular kidney and healthy large arteries than with atheromatous arteries and healthy kidneys. He also shows that the hypertrophy of the ventricle, which results from degeneration of the arteries alone, is less in amount than that which is often associated with disease of the kidney while the large arteries are healthy. This result might have been inferred from the experiments on apnœa referred to in my last lecture. For, since it has been proved that the combined force of contraction in the muscular arterioles is greater than that of the ventricle, it is evident that the contracting arterioles would impede the circulation, and so

add to the work of the ventricle in a greater degree than the degeneration and impaired elasticity of the large arteries.

In the advanced stages of renal degeneration, some of the muscular arterioles may undergo degenerative changes, partly perhaps due to the impure blood which they transmit, and partly to the excessive strain to which they are subjected by the forcible contraction of the hypertrophied heart. In the so-called lardaceous form of renal disease, the muscular arterioles very early undergo this degenerative change, and, their contractile power being thus impaired, they are unable to regulate or to impede the circulation. Hence it happens that hypertrophy of the heart is rarely associated with this lardaceous form of disease.

Amongst the accidental injuries which result from the high arterial tension associated with renal disease, one of the most frequent and most serious is the occurrence of *rupture of one or more intracranial arteries*, and consequent hæmorrhage into the substance or on the surface of the brain. It has been a debated question with some writers on cerebral hæmorrhage, whether the occurrence of that accident is favoured by hypertrophy of the left ventricle. When hypertrophy of the heart is a result of disease of the aortic valves, or of degeneration with impaired elasticity of the walls of the large arteries, it is generally no more than sufficient to overcome the impediment thus offered to the circulation. The strength of the left ventricle, therefore, in such cases is not a true measure of the force with which the blood is sent into the distal arteries. On the contrary, it is a measure of the difficulty with which the blood is transmitted through the primary branches, and, therefore, through the entire system of arteries. When hypertrophy, thus originating, is associated, as it sometimes is, with cerebral hæmorrhage, the reason is that the hypertrophy and the hæmorrhage are joint results of one common cause, namely, degeneration pervading more or less extensively the arterial tree. The hypertrophy of the left ventricle is a consequence of degeneration of the aorta and its primary branches. The cerebral hæmorrhage is a consequence of a similar degeneration of the arteries of the brain.

The state of the circulation is very different when the left ventricle has become hypertrophied, in consequence of the impediment resulting from contraction of the hypertrophied muscular arterioles in connection with degeneration of the kidney. In this state of things, while the arterial stopcocks are resisting the passage of the morbid blood, the strong left ventricle is forcibly driving it onwards. There is thus an excessive strain upon the whole length of the arterial pipes, between

the stopcocks and the cardiac forcing-pump. One of the bits of arterial tubing being overstretched, becomes brittle, and breaks ; then the powerful ventricle forces the blood through the ruptured artery into the yielding tissue of the brain, and a rapidly fatal sanguineous apoplexy is the result. It is a well known fact that some of the most formidable cases of cerebral hæmorrhage are those which are associated with granular contraction of the kidney.

Here it may be convenient to discuss the phenomena called *reduplication or doubling of the first sound of the heart*, which many observers have noted as being one of the most frequent results of the high arterial tension associated with various forms and stages of Bright's disease. Dr. Sibson devoted much time and labour to the investigation of this physical sign of arterial tension, and he discussed it at length in his Lumleian lectures. He explains the reduplication of the first sound by stating that the left ventricle, owing to the resistance offered by the tight arteries to the expulsion of its contents, continues its contraction later than the right, which has expelled its blood into the pulmonary artery with comparative ease. The shock of the first sound is heard at the end of the contraction of the ventricle. Hence, in consequence of the left ventricle contracting more tardily than the right, there is a doubling of the first sound.

Dr. Sibson admits that there is a difficulty in reconciling this explanation of doubling of the first sound with the absence of doubling of the second sound in the same cases. If the left ventricle contract more slowly than the right, so that the sound of the two ventricles is separated by an appreciable interval, it would seem that the aortic valves must close later than the pulmonary, and there should be a double second as well as a double first sound. Dr. Sibson endeavoured to meet this difficulty by the following argument. "In these cases, the systemic arteries are always in a state of great tension. When the blood ceases to be sent into the tight aorta, the instant contraction of the walls of the arteries sends the blood back upon the aortic walls and valve. The pulmonary arteries, at the commencement of the systole, are comparatively flaccid, but become tense at the end of it. The walls of the pulmonary artery begin to contract and send back a return wave again upon the trunk of the artery ; but, as these walls are not always in a state of tension, they take a longer time to contract than those of the aorta and its branches. Owing, therefore, to the slowness of the pulmonary and the quickness of the aortic contraction, the latter, which is already heavily handicapped, makes up in speed what it loses in

time, and the two systems of arteries deliver their back-stroke at the same instant."

Now, it seems to me that this explanation, while it apparently removes one difficulty, raises another of a very formidable character. If the greater tension of the aorta, in the cases of renal disease under consideration, enable it to overtake the earlier but less rapidly and forcibly contracting pulmonary artery, it seems obvious that, in the normal condition, when the aorta and the pulmonary artery commence their elastic contractions at the same instant, the much greater tension of the aorta, with its thicker and stronger walls, should react upon and close its valves before those of the more feebly contracting pulmonary artery are closed, and the result would be reduplication of the second sound as a constant and normal condition. During the last two years, since my attention has been particularly directed to this subject, I have met with numerous instances of an analogous doubling of the first sound in cases of general emphysema of the lungs, with impeded pulmonary circulation and resulting fulness and hypertrophy on the right side of the heart. In these cases, the increased tension of the pulmonary artery consequent on the obstruction in the lungs can never equal the normal tension of the aorta. However great may be the hypertrophy of the right ventricle in cases of emphysema, the thickness of its wall is never equal to that of the left ventricle. If, then, in accordance with Dr. Sibson's theory of asynchronous ventricular contraction, the right ventricle, in consequence of increased tension in the pulmonary artery, complete its contraction later than the left, and thus cause the doubling of the first sound, the closing of the pulmonary valves must inevitably be effected later than that of the aortic, and the second sound must also be doubled. The reverse, however, is the case. The second sound is single in these cases of emphysema, while the first is distinctly reduplicated.

There are anatomical difficulties in the way of accepting the theory of an asynchronous contraction of the ventricles in explanation of doubling of the first sound. The muscular fibres of the two ventricles pass from one side to the other and interlace in such a manner as appears to render the synchronous contraction of the ventricles a physical necessity. And, in watching the exposed heart of a living animal in the different stages of apnœa—first, in the stage of systemic obstruction, with distension of the left cavities, and later, during the period of pulmonary obstruction, with great distension of the right cavities and comparative emptiness of the left—I have particularly ob-

served the uninterrupted exact synchronism of the contractions on the two sides.

A consideration of the difficulties which present themselves in relation to Dr. Sibson's theory of reduplication of the first sound in connection with Bright's disease led me to seek for another explanation of the phenomena ;* and last year I ventured publicly to suggest that the true explanation is to be found in the fact that *the contraction of a dilated, and especially of an hypertrophied auricle becomes audible, and thus the first division of the double first sound in the cases under consideration is the result of the auricular systole.* I believe that this explanation of reduplication of the first sound will be found consistent with all the ascertained facts. I was led up to this explanation by observing that the rhythm of the heart's sounds in cases of reduplication is precisely the same as that of the triple pericardial friction-sound which may often be heard in cases of pericarditis, the first element of the triple friction-sound being caused by the systole of one or both auricles roughened by lymph.

This triple pericardial friction-sound may require here a few words of explanation. For some years past, when describing the friction-sound of pericarditis, I have been in the habit of speaking of it as not merely double—to-and-fro—but, in a large proportion of cases, as triple, a third sound often intervening somewhere between the other two. I said "somewhere", because until recently I could not tell at what period of the heart's revolution the third sound occurred. I got the first hint towards the solution of the problem from a very interesting clinical lecture published by the late Dr. Hyde Salter (*Lancet*, July 29th, 1871, p. 151). In that lecture, Dr. Salter described a case of rheumatic pericarditis, in which a friction-sound double over the mid-sternum became triple over the right third intercostal space, close to the sternum ; and, as this triple character of the friction-sound was most marked when the stethoscope was placed directly over the right auricle, Dr. Salter said : " I feel no doubt that the third element of the sound, on passing from the surface of the ventricle to that of the auricle, is due to auricular pericardial friction." This patient recovered.

In a second case of renal pericarditis related by Dr. Salter, a single pericardial friction-sound of distinctly presystolic—that is, auricular systolic—rhythm was heard over the third costal cartilage, about an inch to the left of the sternum; and, the patient dying a few days after-

* A Clinical Lecture on Triple Pericardial Friction-Sound, and on Reduplication of the First Sound of the Heart (*Lancet*, May 13th, 1876).

wards, the left auricle was found covered and roughened by lymph. "The roughening was confined to the surface of the auricle, and, therefore", Dr. Salter remarks, "the friction-sound coincided with the movements of the auricle."

Not long after the publication of Dr. Salter's lecture, a man was admitted under my care with granular kidney in an advanced stage. A few days after his admission, I noted a presystolic friction-sound, most distinct between the left nipple and the sternum; and, as the sound was evidently synchronous with the auricular systole, I stated at the bedside that it was probably caused by recent lymph on the surface of one auricle. Three days later, in addition to the presystolic friction before noted, there was a systolic friction-sound heard most distinctly over the apex of the heart, just to the left of the mammary line, the heart being enlarged. I then expressed my belief that, besides the roughening of the auricle by lymph, there was a patch of lymph near the apex of the ventricle. In the course of about a month, first the presystolic friction ceased to be heard, and then the systolic friction ceased and was replaced by a systolic blowing murmur at the apex. The patient died after being rather more than two months in the hospital; and, at the inspection, we found, as we had expected, that the right auricle and the apex of the right and left ventricles were covered by lymph, the smoothing down of the surface of which by friction accounted for the cessation of the friction-sounds which were distinctly audible when the surfaces were roughened by recent exudation. The margins of the mitral valve were thickened by lymph, and thus the regurgitant mitral murmur was explained.

And now, having learned from the study of Dr. Salter's recorded cases, and from the observation of this one case under my own care, that an auricle covered by lymph may cause a friction-sound of presystolic rhythm, I saw that in this sonorous influence of the contracting auricle was to be found the interpretation of the triple friction-sound of pericarditis with which I had long been familiar as a clinical fact, although I had not heretofore been able to explain it.

When the general surface of the heart, including both auricles and ventricles, is covered by recent lymph, the friction-sound is distinctly triple, *rub-rub-rub*, reminding one, as Dr. Salter says, of the triple sound of a canter. The first two divisions of the triple sound occur in quick succession, the third after a longer interval; then follows a pause, and again the *rub-rub-rub* occurs. Now, if, while we are listening to this triple sound, we place our finger over the heart's apex, or

over one carotid artery, and at the same time bear in mind what we have seen of the rhythmical contractions of the exposed heart of a living or a recently dead animal, we can readily perceive that the first element of the triple sound is auricular systolic, the second ventricular systolic, and the third ventricular diastolic ; while the silent interval which follows coincides in time with the post-diastolic pause. The relation of the triple friction-sound to the heart's movements may be represented as follows.

Rub — Auricular systole.
Rub — Ventricular systole.
Rub — Ventricular diastole.

Rub — Auricular systole.
Rub — Ventricular systole.
Rub — Ventricular diastole.

I have thus briefly referred to the triple friction-sound of pericarditis, for the purpose of pointing out that the rhythm of the heart's sounds in a case of reduplication of the first sound is precisely the same as that of the triple friction-sound. The triple friction-sound being represented by *rub-rub-rub*, the triple sounds in a case of reduplication may be expressed by *rat-tat-tat*. The cautering character of the sounds may be imitated by bringing down sharply upon the table in quick succession the ends of three flexed fingers, making the two first taps nearer together than the second and third. The friction-sounds are longer and more nearly continuous, but I repeat that the rhythm is precisely the same in the two classes of cases. The relation of the triple sound to the heart's movements may be represented as follows.

Rat — Auricular systole.
Tat — Ventricular systole.
Tat — Ventricular diastole.

Rat — Auricular systole.
Tat — Ventricular systole.
Tat — Ventricular diastole.

The reduplication of the first sound in cases of Bright's disease is usually heard most distinctly between the mamma and the sternum in the third left intercostal space ; that is about the line of junction be-

tween the auricle and ventricle. The sound may be single or indistinctly double at the apex, while it is decidedly double at the third interspace and again single over the aorta. This statement of the position in which the reduplication is best heard accords with Dr. Sibson's account; but our explanations differ essentially. He states that, in this position, the asynchronous contraction of the two ventricles is best heard, while I maintain that the contraction of the tense, dilated, and often hypertrophied auricle is there heard immediately before the sound of the ventricular systole.

The question then arises, Does the contraction of the auricle afford a satisfactory explanation of the first division of the reduplicate sound? I believe that it does. It is of course admitted that in the normal state the contraction of the auricle, contrary to Laennec's original theory of the heart's sounds, is inaudible; but we have positive evidence of sound resulting from the auricular systole in two distinct morbid states. First, as a result of constriction of the mitral orifice, we have the now well-known presystolic—or, as Dr. Gairdner happily designates it—the auricular systolic mitral murmur. In these cases, the impediment resulting from mitral constriction causes a slow but forcible auricular systole with a resulting presystolic, that is, preventricular systolic murmur, followed by a short first sound, the result of rapid contraction of the partially filled left ventricle. Second, when the surface of an auricle is roughened by lymph, there occurs the presystolic, or rather the auricular systolic friction-sound. Third, as a result of obstruction in the systemic arteries, and consequent distension of the left auricle, either with or without hypertrophy of its walls, we have, as I believe, an audible auricular systole, constituting the first division of the reduplicate first sound in cases of Bright's disease. The rhythm of this auricular systolic sound—its place in the heart's revolution—is precisely the same as that of the auricular systolic mitral murmur, and of the auricular systolic pericardial friction-sound; and this identity of rhythm in the three classes of cases affords one of the strongest proofs that the sound in each case is caused by the auricular systole. The triple friction-sound of pericarditis, and the triple sound associated with doubling of the first sound, are alike suggestive of a canter.

I have before stated that the reduplication of the first sound occurs not only in connection with Bright's disease, but it is very commonly associated with the impeded pulmonary circulation resulting from advanced general emphysema of the lung. I have observed it frequently in elderly persons with degeneration and rigidity of the arterial walls; also very

distinctly above and to the right of the left nipple in some cases of mitral regurgitation. There is one feature which is common to all these cases, and that is an impeded circulation either pulmonary or systemic, and the obstruction acting backwards causes distension, and by degrees hypertrophy of one or both auricles. It is obvious that an impediment commencing in the systemic arteries, or on the left side of the heart, may by a retrograde influence extend through the lungs to the right cavities of the heart.

In some cases of coexisting emphysema of the lungs and chronic Bright's disease, both sides of the heart become simultaneously hypertrophied, and the reduplication of the first sound is distinctly heard over an extensive surface. During the last year I have seen several examples of this complication. It is obvious that the theory of asynchronous ventricular contraction entirely fails to explain the reduplication which results from a simultaneous—equal or nearly equal—impediment in the systemic and in the pulmonary vessels. An equal retardation of the two ventricles would not throw one behind the other. But the auricular theory completely explains the phenomena. That a distended and especially an hypertrophied auricle should produce sound by its contraction, is quite consistent with what we know of the causation of the normal sounds of the heart. While the first sound is caused by the tension of the ventricular walls and the auriculo-ventricular valves during the systole of the ventricle, the second sound results from the sudden tension and vibration of the arterial valves and walls during the diastole of the ventricle. In like manner, it is maintained that when, in consequence of excessive arterial pressure, there is great distension of the heart's cavities, the tense auricle contracts audibly and causes the earlier division of the double first sound, the double sound being the result of the auriculo-ventricular systole.

That the contraction of the terminal muscular arterioles, excited by blood-contamination, the result of renal disease, should act backwards through the systemic arteries to the left ventricle and auricle, so as to cause an appreciable modification of the heart's sounds, and ultimately hypertrophy of the muscular tissue of the propelling heart and of the resisting and regulating arterioles, is an interesting illustration of the correlation of physiological forces and of the intimate relation between physiology and pathology.

In confirmation of the explanation which I have given of the so-called reduplication of the first sound, I may mention that, after I had

written the lecture in which I first publicly propounded this theory, my attention was directed to a recently published thesis by Dr. Exchaquet of Paris, entitled *D'un Phènomène Stethoscopique propre à certaines Formes d'Hypertrophie du Cœur*, in which I found that my explanation of the phenomena had been anticipated.

The author of the thesis gives the results of numerous observations made by his teacher Dr. Potain on that modification of the heart's sounds which Dr. Sibson called reduplication, but which the French observers designate *bruit-de-galop*. Dr. Exchaquet quotes Dr. Sibson's Lumleian Lecture, raises various strong objections to his theory of asynchronous ventricular contraction, and maintains that the presystolic element of the double first sound is caused by *an abnormally energetic and forcible contraction of the left auricle.* I was much interested to find that my explanation, arrived at quite independently, had thus been anticipated and confirmed by Dr. Potain, who points out that, when the chest is not thickly covered by fat, the presystolic contraction of the auricle may be seen and felt in the third left intercostal space, where, in the same cases, the *bruit-de-galop* is also most distinctly heard.

I find, however, that Dr. Potain looks upon this modification of the heart-sounds as being almost invariably associated with certain forms ot albuminuria. As an exaggeration of a normal phenomenon, he has observed it to a very slight degree, and as a transient condition in persons free from organic disease and from functional disorder of any kind; but when the *bruit-de-galop* is pronounced and permanent, he believes it to be invariably associated with albuminuria and resulting distension of the left auricle; and, in fact, he looks upon this acoustic sign as diagnostic of certain forms of albuminuria. The author makes no reference to the very frequent association of the *bruit-de-galop* or doubling of the first sound with emphysema, and other conditions, resulting in an impeded circulation through the lungs, and consequent distension of the right auricle, but often unassociated with albuminuria : a class of cases of very common occurrence to which I have directed attention in this lecture.

The reduplication of the first sound, upon the interpretation of which I have dwelt so long, is not without its practical prognostic significance and value, in so far as it affords undoubted physical evidence that the impediment to the circulation, whether in the pulmonary or in the systemic vessels, is acting backward through the ventricle upon its associated auricle, and is causing some degree of auricular dilatation and

hypertrophy; and, on the other hand, the cessation of the reduplication, as, for instance, in some cases of acute and transient Bright's disease, is evidence of returning freedom of the circulation, and is thus far of favourable omen.

Again, it is obviously important to observe and study this peculiar modification of the heart-sounds with sufficient care to distinguish it from any form of valvular murmur. I do not doubt that a modification of reduplication, by which the two first elements of the triple sound are blended together, so as to give the first sound of the heart a prolonged character, has often been mistaken for the murmur of mitral regurgitation; and this error of observation has been made the basis of an alarming, but wrong, prognosis. I scarcely need add that our interest and our duty alike prompt us to avoid so serious a mistake.

Lecture III.

Renal Asthma: Symptoms and Proximate Cause.—The Dry and Inactive Skin of Bright's Disease: its Proximate Cause.—Is Diuresis a Result of High Arterial Tension?—Is High Arterial Tension a Cause of Albuminuria?—Uræmic Convulsions and other Nervous Symptoms: their Relation to Epilepsy: their Proximate Cause: Principles of Treatment.—Two Forms of Impaired Vision in Bright's Disease: the Proximate Cause of each.—Cholera Collapse and Pulmonary Embolism compared.—Cholera Collapse and Spasmodic Asthma compared.—Conclusion.

There yet remain for consideration certain symptoms and results of renal disease which are more or less intimately associated with and dependent upon those impediments and derangements of the circulation to which I directed special attention in my last lecture; and amongst these symptoms there is a peculiar form of dyspnœa, or, as it is sometimes called, *renal asthma*. During the progress of the various forms of renal degeneration which are commonly included under the generic term Bright's disease, a more or less persistent dyspnœa may result from a variety of causes, such as anæmia with a deficiency of the oxygen-carrying hæmatine; bronchitis or œdema of the lungs; fluid in the pleura, or in the pericardium, or in the abdomen; an enfeebled condition of the heart, either with or without valvular disease. But the dyspnœa to which I now refer is of a different character. It is not persistent, but occasional and intermittent, coming on in paroxysms, in some cases soon after food has been taken, and especially after an evening meal; while in other instances it occurs mainly during the night, when it entirely prevents or greatly disturbs the patient's sleep. In some cases, the attack resembles one of spasmodic asthma, and there are loud sibilant *râles* over the lungs, apparently the result of bronchial spasm; but in the more typical cases the phenomena are quite different. The breathing is hurried and laborious, the heart's action is rapid and feeble, and there is more or less lividity of the lips and of the general surface; yet, on auscultation, loud puerile respiration, unmixed with *râles* or crepitation, may be heard over the whole of both lungs; while in other cases, especially after a long continuance

of the dyspnœa, fine crepitation may be heard over the bases of the lungs, but there is obviously no deficiency of respired air, nor any change in the physical condition of the air-passages to explain the distressing symptoms. It can scarcely be doubted that the symptoms in question are the result of a form of uræmia; and they occur with especial frequency in the advanced stages of the contracted granular kidney, with which other forms of uræmic poisoning are so commonly associated.

The question then arises, What is the proximate cause of this uræmic dyspnœa? We know that dyspnœa—a distressing sense of suffocation—arises when, from any cause, the free intermingling of the blood with the respired air is prevented. The respiratory process may be interfered with alike either by an obstruction in the air-tubes hindering the access of air to the pulmonary cells, or by some impediment to the onward flow of blood through the pulmonary capillaries. A plug in the pulmonary artery causes a sense of suffocation as urgent and distressing as an obstruction in the larynx, trachea, or bronchial tubes. I have on several occasions had the opportunity of observing the symptoms which result from an embolon or a thrombus in the pulmonary artery. When the obstruction of the artery is sudden and complete, there is usually a combination of pallor with lividity of the surface, the result of systemic venous fulness, epileptiform convulsions consequent on sudden extreme arterial anæmia of the brain, and death within a few seconds or minutes from arrest of the circulation. When the obstruction of the pulmonary artery is less complete, but permanent, and sufficient to destroy life, the respiration is hurried and laborious, and attended with a distressing feeling of want of breath. One poor girl, who was dying from this cause, panted out the statement, "I feel as if I could not get breath enough"; yet over the whole of both lungs, except over two limited patches where some blood had become impacted in the terminal bronchi, there were unimpaired resonance and loud puerile respiration. The surface of the body in these cases becomes cold and pallid, with more or less lividity of the lips; and the pulse is small and feeble, or even quite imperceptible.

It is obvious that the blood-current through the lungs is the channel by which oxygen reaches the tissues; and, when that current is obstructed, the sense of breathlessness is the result of a call from the tissues for the indispensable vitalising oxygen.

Now, it has occurred to me that the paroxysmal dyspnœa of Bright's disease may be, in part at least, explained by an interrupted circula-

tion through the pulmonary capillaries occasioned by spasm of the pulmonary arterioles, which are stimulated to this excessive contraction by the influence of the impure blood upon the vaso-motor nerves and centre. There are some facts and arguments which support this theory of the pathology of renal asthma.

The panting laborious mode of breathing and the sense of breathlessness are very like the symptoms which result from a plug narrowing but not completely obstructing the pulmonary artery. A consideration of the *juvantia* and *lædentia* lends support to the theory of arterial spasm in the lungs. In some cases, the dyspnœa is speedily and greatly relieved for the time by inhaling the vapour of nitrite of amyl; and this relief is probably due to the well-known influence of this agent in relaxing the muscular arterioles. In many instances, relief is afforded by moderate doses of chloral-hydrate, either alone or in combination with bromide of potassium. Ten grains of each of these compounds may be given twice or thrice in the twenty-four hours, This combination probably acts by lessening the reflex excitability of the vaso-motor centre. If, however, the secretion of urine be very scanty, and the blood consequently much contaminated by retained excreta, the chloral may fail to relieve, and it may even add to the distress. In this condition, the breathing is often most effectually relieved by means directed towards the purification of the blood by promoting the free action of the skin and bowels, while the diet is carefully regulated both as regards quantity and quality, an exclusive milk-diet being often the most suitable. The dyspnœa is almost invariably made worse by opium in any form; and the probable explanation of this is, that opiates, by checking the secretions of the bowels and kidneys, increase the blood-contamination, and thus intensify the exciting cause of the dyspnœa.

My late distinguished friend and colleague Sir William Fergusson often discussed with Sir George Burrows and me the etiology and treatment of this distressing symptom, from which he himself suffered severely during the last few weeks of his life. He asked me if I could explain the dyspnœa, and I suggested to him the explanation which I have just now given. He said that my explanation appeared to be in accordance with his own sensation, which was that of an obstruction somewhere within the chest; and, as the obstruction was evidently not in the air-passages or in any of the heart's orifices, it seemed probable that it might be in the pulmonary arteries. He several times described to me an interesting observation which he had repeatedly made upon

himself. He found that, by voluntarily increasing to the utmost the respiratory movements—that is, making forcible inspirations and expirations fifteen or twenty times in succession—he could for a time free himself almost entirely from the distressing sensation of breathlessness. Then gradually, in the course of a minute or two after the cessation of the forced respirations, the former feeling of want of air returned; and he explained the temporary relief by suggesting that the deep inspirations had the effect of sending on a larger volume of blood highly charged with air.

The theory of uræmic dyspnœa which I have here set forth receives some confirmation from one fact which I have frequently observed. I allude to the fact that, when the dyspnœa has been long continued or has frequently recurred, although the respiratory sounds may have been quite pure and free from crepitating *râles* at the commencement, yet sooner or later moist wheezing sounds may be heard over the bases of the lungs at the back. The explanation which I would suggest is the following. In consequence of the impeded passage of blood through the minute pulmonary arteries, there is an unusual distension of the right cavities of the heart and of the systemic venous trunks. The bronchial veins, which open through the vena azygos and the superior intercostal vein into the superior cava, participate in this distension; and, in consequence of the engorgement of the bronchial veins and capillaries, there occurs a passive serous exudation into the bronchial tubes, which, gravitating towards the bases of the lungs, gives rise to the moist crepitating sounds which are heard there. A similar engorgement of the bronchial veins and capillaries occurs as a result of the impeded pulmonary circulation consequent on the various forms of apnœa, whether the cause of the apnœa be the bronchial spasm of spasmodic asthma, obstruction of the larynx by diphtheritic false membrane, compression of one lung by a rapid and copious effusion, or extensive pneumonic consolidation of one lung. In a case of rapidly fatal laryngeal diphtheria, the contrast between the extreme anæmia of the pulmonary capillaries and the excessive capillary and venous engorgement of the bronchial mucous membrane is very striking. The explanation is obvious. In proportion to the exclusion of air from the lungs, the pulmonary arterioles contract and the capillaries are anæmic, and in the same proportion the blood accumulates in the trunks of the pulmonary artery, in the right cavities of the heart, and in the systemic veins, including the bronchial veins and capillaries; and so the bronchial mucous membrane is congested. The

dark colour of the lungs noted in some cases of sudden apnœa—as, for instance, in Dr. Massey's case of hanging quoted in my first lecture—is explained by the engorgement of the bronchial veins and capillaries consequent on the arrested circulation through the pulmonary arterioles.

The hæmoptysis which sometimes follows a severe and prolonged attack of spasmodic asthma is probably explained by rupture of the overgorged bronchial capillaries consequent on the obstruction in the pulmonary arterioles which results from the bronchial spasm. The order of events is, first, bronchial spasm, with resulting partial apnœa; second, contraction of the pulmonary arterioles, with a backward engorgement extending to the bronchial veins and capillaries, which may relieve themselves by a sero-mucous exudation or by actual rupture and hæmorrhage.

Another phenomenon closely allied to this is the œdema of the sound lung, which occurs not unfrequently when one lung has been suddenly consolidated by pneumonia or compressed by a rapid and copious pleuritic effusion. In such a case, moist crepitating sounds may often be heard in the bronchi of the healthy lung: a condition of things which must always be looked upon with anxiety, because an increase of this œdematous effusion into the bronchi may cause a fatal apnœa. There can, I think, be no doubt that the bronchial, and not the pulmonary, vessels are the source of this serous exudation. In consequence of the impervious condition of the inflamed lung, there is a state of partial apnœa; more blood is sent to the sound lung than can be fully aërated; its progress is checked and regulated by the stop-cock action of the pulmonary arterioles; the right cavities of the heart and the systemic veins are engorged; and with this there is bronchial venous and capillary congestion, and a consequent passive serous exudation into the bronchi. In the condition here described, a timely venesection may sometimes rescue the patient from impending suffocation. The abstraction of blood relieves the distension of the veins and the right cavities of the heart, and at the same time it lessens the work of the lung in proportion as the volume of blood to be aërated is diminished.

A case of tricuspid regurgitation, which came under my care some years ago at the hospital, affords an instructive illustration of the effect of an impediment originating at the right side of the heart acting backwards, first upon the bronchial, and secondly upon the pulmonary, circulation. A woman, aged 52, was admitted with general dropsy,

albuminuria, a systolic bellows-sound at the bottom of the sternum (*i.e.*, over the tricuspid valve), distended and pulsating jugulars, and the physical signs of bronchitis. A single dose of elaterium, acting very freely upon the bowels, removed at once the dropsy, the albuminuria, and the bronchial *râles*. After a few days, however, all the symptoms returned, and the patient soon died. We found, as we had expected, dilatation of the tricuspid orifice so great, that the valve was incompetent to close it; while all the other valves and orifices were normal. The lungs were much engorged. In this case, it is evident that the primary cause of all the symptoms was incompetence of the tricuspid valve. There was consequently reflux of blood into the systemic veins, renal congestion and albuminuria, anasarca, bronchial venous and capillary congestion with a muco-serous exudation into the bronchi, and then a secondary obstruction in the pulmonary capillaries consequent on the pressure of the gravitating bronchial secretion.

It is interesting to note that, on one occasion before her admission, she had spat some blood, the source of which was, in all probability, the overgorged bronchial capillaries. We are familiar enough with hæmoptysis as a result of mitral constriction or incompetence, the source of such hæmoptysis being, in most instances, the pulmonary vessels; but disease on the right side of the heart obviously throws back the strain and pressure primarily and chiefly upon the bronchial vessels.

One of the most constant symptoms and results of chronic Bright's disease is a remarkably dry, harsh, and inactive state of the skin; a state of skin which, in many instances, resists even the diaphoretic influence of the hot-air or the Turkish bath. I formerly supposed, and publicly expressed my belief, that this condition of skin might be due to the fact that the excessive contraction of the hypertrophied subcutaneous arterioles resists the relaxing effect of external warmth which has so powerful a diaphoretic influence upon the healthy skin. My belief was that the deficient cutaneous secretion was a result of a defective blood-supply to the sweat-glands. I take this opportunity of saying that, for some time past, I have abandoned this theory as unsatisfactory and erroneous. It must be borne in mind that the excessive power of resistance possessed by the hypertrophied arterioles is to a great extent, if not entirely, compensated by the increased injecting force of the hypertrophied left ventricle. The inactivity of the skin, therefore, is not to be explained by a defective blood-supply. I now

believe that the dry and inactive state of the skin, which is commonly associated with chronic renal disease, is to be sought for in a structurally diseased condition of the sweat-glands themselves. With the able assistance of my colleague Professor Gerald Yeo, I hope ere long to be able to demonstrate as a fact what is now only a plausible hypothesis, but one which is rendered probable by some well ascertained facts. We know that disease of one excretory organ frequently induces disease in one or more allied organs. For example, when, in consequence of obstruction of the gall-duct, or some structural disease of the liver, bile accumulates in the blood, the products of that secretion are vicariously eliminated by the kidneys, and the result is that the secretory tissues of the kidney undergo structural changes. The urine is not only deeply tinged with bile, but it is often found to contain desquamated renal epithelium, tube-casts, and sometimes albumen. The excretion of biliary materials excites a mild form of desquamative nephritis.

It is notorious that suppressed action of the skin by exposure to cold and wet is a very common cause of acute renal disease with albuminuria. The most probable explanation is that the products of the cutaneous secretion, being retained in the blood, are partially excreted by the kidney, and excite structural changes there, as bile-products have been shown to do. There is a very close relationship and interdependence between the cutaneous and the renal secretion. Many of the symptoms of uræmic poisoning may be removed or mitigated if by any means we can promote and maintain a free action of the skin, the prolonged application of the wet pack being one of the most efficacious of these means. Now, there is reason to believe that when, in consequence of degeneration of the kidney, urinary materials accumulate in the blood and are partly excreted by the skin, as they have been proved to be, this vicarious excretion will induce structural changes in the sweat-glands, and thus explain the abnormal dryness of the skin. This, which is at present a theory, I expect soon to see as a demonstrated fact; and if any one or more workers will take up this subject and complete the demonstration before Dr. Yeo and myself have had the opportunity of doing it, we shall be very happy to be thus anticipated.

Another symptom, which some writers on renal pathology have, as I think erroneously, attributed to increased vascular tension, is the copious secretion of urine which is often associated with the small granular kidney. It is possible, though by no means certain, that in-

creased pressure on the *capillaries* of the kidney might cause a more copious secretion of urine ; but, in the granular kidney, the firm contraction of the hypertrophied renal arterioles counteracts the injecting force of the strong left ventricle, and thus prevents an increased afflux of blood into the capillaries of the kidney. There is no reason to suppose that high arterial tension has any direct tendency to cause an increased secretion of urine. In cases of contracted granular kidney, the two conditions are associated, but in the early stages of the lardaceous kidney the copious secretion of urine occurs without arterial tension. It is probable that in both classes of cases the copious flow of urine is caused by the diuretic influence upon the kidney of some abnormal products in the circulation ; an influence analogous to that of sugar in cases of diabetes.

Again, it has been supposed by some that vascular tension may be a direct physical cause of albuminuria. But if, as we have good reason for believing, the increased vascular tension is a result of resistance caused by contraction of the arterioles, it is evident that, just in proportion as the renal arterioles contract and resist the blood-stream, the pressure in the capillaries in front of them will be lessened. And it is a matter of daily experience that in those cases of chronic renal disease which are commonly associated with the highest degree of arterial tension—cases of small granular kidney—the amount of albumen in the urine is least, and not infrequently there is none, even in the advanced stages of the disease.

Relaxation of the renal arterioles is more likely to cause albuminuria than their excessive contraction ; and the late Dr. Warburton Begbie published some cases in which he believed that the urine became albuminous in consequence of vaso-motor paralysis, resulting in an increased afflux of blood to the Malpighian capillaries.

This view, too, is confirmed by the results of experiments. Vulpian (vol. i, p. 534) describes the effect of dividing the left splanchnic nerve of a dog just above the kidney. The renal arterioles being paralysed, the kidney at once becomes congested, red, and swollen, the quantity of urine excreted by that kidney is increased, and it becomes highly albuminous. Then galvanisation of the distal end of the divided nerve stimulates the renal arterioles to contract, and the red and congested kidney gradually becomes pale.

Contraction of the systemic arterioles in general, with relaxation of the renal arterioles, might cause capillary renal congestion and albu-

minuria; but this is not the condition which exists in cases of chronic albuminuria with high arterial tension. On the contrary, there is evidence that the renal arterioles in these cases are more firmly contracted and more decidedly hypertrophied than those of any other organ or tissue.

An *impediment* to the circulation causing albuminuria must act *in front* of the Malpighian capillaries, so as to cause a backward engorgement and a transudation of serum through their walls into the uriniferous tubes. Thus, Dr. George Robinson (*Med.-Chir. Trans.*, vol. xxvi, p. 51) proved many years ago that a ligature on the renal vein of a living rabbit renders the urine albuminous, and even bloody. This experiment has been repeated by Frerichs and others with the same result. Bowman's demonstration of the structure of the Malpighian bodies and their connection with the uriniferous tubes rendered these results quite intelligible. In like manner, distension of the convoluted tubes by morbid exudation within them may, by compressing the intertubular capillaries, cause engorgement of the Malpighian capillaries and escape of serum through their walls.

There is good reason to believe that some of the more formidable *nervous symptoms* which result from uræmia—in particular uræmic convulsions and a form of transient amaurosis—are directly due to cerebral anæmia consequent on sudden extreme contraction of the muscular arterioles.

There can, of course, be no question that uræmic convulsions are of an epileptic character. A large amount of evidence points to the conclusion that both the loss of consciousness and the convulsions of epilepsy are the results of sudden and extreme anæmia of the brain, In man, and in most, if not in all, warm-blooded animals, a rapid and very copious hæmorrhage usually causes convulsions. Kussmaul and Tenner state (*On the Nature and Origin of Epileptiform Convulsions caused by Profuse Bleeding*, New Sydenham Society, 1859) that in numerous cases of dogs, cats, and rabbits, they observed, without a single exception, violent and general convulsions preceding death by loss of blood. In order to produce this result, the hæmorrhage must be rapid. If it occur slowly, so that the vital powers are gradually exhausted, death then occurs with swooning, drowsiness, and delirium without convulsions.

The same experimenters found that an interruption of the supply of blood to the head of a rabbit, by ligature or compression of the arteries of the neck, produces epileptic convulsions as surely as hæmorrhage

does. In about one hundred rabbits they ligatured or compressed the carotids and subclavians, from which, be it remembered, the vertebral arteries proceed ; and in every case, except that of one very old lean and feeble animal, convulsions occurred.

In order to excite convulsions, they found it necessary to close all the four arteries which supply the brain. If but one carotid or one vertebral artery remained pervious, the animal was enfeebled and more or less paralysed, but not convulsed. And again, if, during the height of the convulsion, the ligature were removed from one carotid, the convulsions generally ceased immediately, and there was a sudden change from the most frightful spasm to complete relaxation of the muscles. The description of the convulsions thus artificially produced with, as it seems to me, needless reiteration, in the lower animals, shows that they were essentially the same as epileptic convulsions in the human subject. There was the dilated pupil, the tonic spasm, quickly followed by clonic convulsion so violent as to throw the animal forward to a distance of one or two feet, and sometimes even over the shoulders of the operator. These experiments obviously could not be performed on the human subject ; but Drs. Kussmaul and Tenner approached as near to this as they dared by compressing the carotids of six men. The result was that in all the face turned pale ; the pupils first contracted and then dilated ; the respiration became slow, deep, and sighing ; then there was giddiness, staggering, and unconsciousness, and the men would have fallen if they had not been supported. They say that, "in two subjects of weak intellect and moderately anæmic, in whom, notwithstanding the above symptoms, the compression was continued, a choking sensation, attended by vomiting and general convulsions, came on, which, however, did not attain an aggravated form ; for, on withholding the compression, they disappeared in a few seconds". (*Op. cit.*, page 28.) Compressing the carotids does not, of course, entirely cut off, but only greatly lessens the supply of arterial blood to the brain ; but these experiments render it probable that sudden occlusion of all the arteries supplying the brain would as certainly excite epileptic convulsions in man as in the lower animals. And this conclusion is confirmed by observing the results of certain diseases and accidents in the human subject. Thus convulsions occur almost invariably as a result of sudden suffocation or acute apnœa. It has commonly been supposed that the convulsions thus occurring are caused by the noxious influence of black blood upon the brain. It is far more probable that they are caused by the sudden and extreme anæmia of the brain, consequent on the im-

peded flow of blood through the lungs into the systemic heart and arteries, as explained in my first lecture. The epileptiform convulsions which often result from the inhalation of nitrous oxide gas admit of the same explanation. It is quite certain that, in Kussmaul and Tenner's rabbits, with closed carotids and subclavians, no black blood could reach the brain, yet the convulsions were apparently identical with those which result from suddenly fatal apnœa, whether in the lower animals or in the human subject.

A few years since, the following case came under the observation of my friend Dr. Lavies and myself. A gentleman, about sixty years of age, had been confined to his bed for three weeks with symptoms which pointed to great feebleness of the heart, and probably to fatty degeneration of its walls. There was dyspnœa on exertion, and sometimes on awaking after a long sleep; the heart's impulse and the radial pulse were feeble; there was some œdema of the legs, and over the bases of the lungs there were moist crepitating sounds, probably the result of œdema there. He awoke in the middle of one night, told the nurse that he felt quite comfortable, asked the time, and began to repeat her reply "Oh, half-past ——", when he suddenly stopped, and the nurse, turning to him immediately, saw that his face was livid and he was in strong convulsions. In a few seconds, and before any one could answer her call for assistance, the patient was dead. The body was examined, in the presence of Dr. Lavies and myself, by my friend and former colleague Dr. Kelly. The walls of the heart were thin, soft, and fat. The right ventricle was dilated and contained a firm decolorised thrombus extending from the apex of the ventricle through the tricuspid orifice into the auricle, to the outer wall of which it had evidently been attached and moulded, but, becoming separated from the auricular wall, it had fallen over the tricuspid orifice and completely closed it. Thus, the circulation must have been completely and instantaneously arrested. The result was lividity of the face from venous fulness, and epileptiform convulsions from cerebral arterial anæmia. In this case, as in the case of the rabbits with ligatured arteries, it is evident that the convulsions were caused, not by black blood, but simply by the absence of circulating blood in the cerebral vessels.

When animals are killed by air being forcibly blown into a vein, the breathing becomes hurried, the animal suddenly falls down, and usually dies in convulsions; the contents of the bladder and rectum being frequently expelled at the time of death. Dr. John Reid states that, "in

very few cases only is death from this cause not preceded by convulsions". *(Physiological, Anatomical, and Pathological Researches.)*

The immediate cause of death in these cases is the arrest of the frothy mixture of air and blood by the contraction of the pulmonary arterioles, the air seldom reaching the left side of the heart; and as a result of this arrest there is, of course, sudden extreme anæmia of the brain, and of every other organ supplied by the systemic arteries. In man, it appears that death from the accidental admission of atmospheric air into a vein during an operation is less frequently preceded by convulsions. Probably the chief reason of the less frequent occurrence of convulsions from this cause in the human subject is, that the amount of air accidentally admitted is less, and death consequently is less rapid than when air is forcibly blown into the vein of an animal. It would probably be found, on a careful inquiry, that the occurrence of convulsions in these cases depends upon the circulation being suddenly and completely arrested.

It has been noted, in some cases of suddenly fatal pulmonary embolism, that death has been preceded by convulsions; and Virchow observed, amongst the results of artificial embolism of the pulmonary artery in animals, convulsions and dilatation of the pupil. *(Des Emboles Pulmonaires*, par B. Ball, page 129.)

We find, then, a large amount of evidence pointing to the conclusion that sudden and extreme anæmia of the brain will cause epileptiform convulsions, and a theory of epilepsy has been framed in accordance with these facts; the theory being that the cerebral anæmia, which is the immediate cause of the convulsion, is the result of spasm of the cerebral arterioles. It may be said with truth that this is only one step towards an explanation of the phenomena, and that the cause of the arterial spasm remains to be determined. We will presently revert to this question.

It is, I think, pretty generally admitted that this theory of cerebral anæmia from arterial spasm is quite consistent with the phenomena of epilepsy. It is a matter of general observation that, at the very commencement of an epileptic fit, the face is pallid. There is obviously anæmia of the superficial vessels, and with this there is probably associated anæmia of the intracranial vessels which supply the brain itself. The pallor is in most cases soon succeeded by lividity, owing to the venous engorgement which results from impeded respiration and pulmonary circulation. It is very remarkable that, while the face is pallid, the heart is beating strongly and the carotids throbbing violently.

These phenomena would be explained by extreme contraction of the muscular arterioles, resisting the escape of blood from the arterial trunks into the capillaries.

Kussmaul and Tenner endeavoured to support the theory of arterial spasm by experiment, and to some extent they succeeded. In each of two white rabbits, they ligatured the two subclavians and one carotid ; the cervical sympathetic, on the other side, was then exposed and galvanised, with a view to excite contraction of the arterioles by the stimulus conveyed through the vaso-motor nerves. In two animals, no effect was produced ; but in the third, the background of the eye became completely pale ; the pupil dilated, so that the iris could scarcely be seen ; the neck was drawn back, and violent convulsions occurred. The electrodes being removed, the spasms ceased, the pupil contracted, and the background of the eye became red ; but the animal continued in a swooning condition. After some minutes, electricity applied to the sympathetic nerve produced the same effect as at first. A third attempt to excite convulsion did not succeed.

The authors suggest that these experiments deserve repetition, with a view of rendering certain what at present is probable, namely, " that epileptic convulsions can be brought about by contraction of the blood-vessels induced by the vaso-motor nerves".

According to this theory, then, epilepsy is the result of sudden anæmia of the brain ; and this anæmia, when not caused by a sudden and profuse hæmorrhage, or by some impediment to the circulation outside the cranium, is due to an extreme contraction of the muscular arterioles. This arterial contraction may be determined by two main classes of causes :

1. By a purely nervous reflex influence, such as, for example, may be excited by anger or terror, by the irritation of the gums during dentition, by a calculus in the kidney, the ureter, or the gall duct, or by worms in the intestines.

2. In the second class of cases, a blood-poison is the exciting cause of the arterial spasm and the resulting epileptic convulsion. This includes all cases in which convulsions result from retained excreta, of which uræmic convulsions are a typical example.

From the preceding narrative of facts, it appears to be highly probable that uræmic convulsions are directly due to a sudden and extreme anæmia of the brain, resulting from contraction of the cerebral arterioles, and that the arterial contraction is excited by the influence of impure blood upon the vaso-motor nerves and centre.

This theory, moreover, indicates two modes in which uræmic convulsions may be prevented, namely : first, by means directed towards removing the morbid quality of the blood ; and, second, by remedies which lessen the reflex excitability of the nervous centre.

Time would not permit, even if it were desirable to enter into the details of treatment ; but I am anxious to direct attention to one or two points of practice. It is a well-known fact that the inhalation of chloroform or ether-vapour invariably puts a stop to uræmic convulsions, and often wards off an attack after premonitory symptoms, such as convulsive twitchings of certain muscles, have occurred. It has sometimes been supposed that the anæsthetic acts by relaxing the cerebral arteries ; but an observation of Kussmaul and Tenner points to a different explanation. These experimenters found that, if animals are etherised, no convulsions occur when they are bled to death or when their intracranial circulation is arrested by ligatures. It appears, therefore, that the anæsthetic vapours prevent or stop convulsions by lessening the reflex excitability of the nervous centre.

The undoubted influence of repeated full doses of bromide of potassium, in warding off uræmic convulsions, is also probably to be explained by its soothing sedative influence on the nervous centres. The bromide is a very useful remedy for the painful muscular cramps which are of common occurrence in the advanced stages of all forms of renal degeneration. These cramps, which are especially frequent and severe in the lower extremities and during the night, are no doubt to be classed with the results of uræmic poisoning, and in not a few cases they are the precursors of more formidable nervous disorder. They may, in some cases, be entirely prevented by a draught containing twenty grains of bromide of potassium, with five grains of carbonate of ammonia, at bed-time.

No doubt, some of the many nervous disorders that result from uræmic poisoning are due to the noxious influence of the morbidly altered blood upon the nervous tissue, while others are more probably explained by sudden partial interruption of the blood-supply to certain parts of the nervous system. This statement may be illustrated by a reference to the two forms of impaired vision, which are very frequently associated with advanced renal degeneration. In one class of cases, dimness of sight comes on more or less gradually, affecting one or both eyes, and is permanent. This form of impaired vision is found to be associated with peculiar structural changes in the retina, results of the

so-called *albuminuric retinitis*. In the other class of cases, the impairment of vision may be so sudden in its onset that, in a few minutes or even seconds, there is complete blindness, which usually passes away as suddenly as it came. These attacks of sudden and transient blindness may recur again and again. That they are closely allied to epileptiform attacks, is shown by the fact that they are sometimes immediately followed by general convulsions. The most probable explanation of this sudden transient form of amaurosis is that which attributes it to sudden anæmia of the retina, or of the central origin of the optic nerves, the result of arterial contraction, excited by the morbid quality of the blood. It is, in fact, a form of circumscribed partial epilepsy, "epilepsy of the retina", as it is sometimes designated.

There are various forms of nervous disorder of uræmic origin which probably admit of a similar explanation: sudden and transient impairment of motor power or irregular spasmodic movements limited to a particular set of muscles; various disordered sensations in limited portions of the skin; sudden perversions of taste, or smell, or sight, or hearing, sudden impairment of speech, vertigo, confusion of thought, temporary mental excitement and delirium. One or more of these symptoms may occur singly or variously associated in different cases, the onset and the departure being often equally sudden. In explanation of these phenomena, Dr. Hughlings Jackson has, with much ingenuity, suggested that they may result from a sudden temporary interruption of the blood-current through one or more branches of the cerebral arteries by spasm of their muscular walls; so that the brain-tissue within a circumscribed "arterial region", having its nutritive supply arrested or limited, would suffer a suspension or impairment of its proper functions. Our increasing experience of the various forms of nervous disorder which may result from so purely mechanical a cause as embolism of cerebral vessels lends support to this theory. An arrest of the circulation through a portion of the brain involves immediate suspension of function in that part, with perhaps a disorderly action in subordinate or correlated parts. Thus, amongst other symptoms of nervous disorder, maniacal delirium, with mental illusions, and acute chorea have been found associated with, and probably have been directly caused by, mechanical plugging of minute cerebral vessels; the plugging being a result of embolic particles of fibrin detached from the so-called warty vegetations on a damaged cardiac valve. In like manner, sudden and complete blindness may result from embolism of the arteria centralis retinæ, partial and patchy blindness from embolism in one of

its branches. The results of the mechanical plugging of vessels are thus seen to bear so strong a resemblance to those which are due to uræmic poisoning as to afford much support to the theory of arterial contraction as the immediate cause of some at least of the characteristic symptoms.

There is another class of cases in which the theory of obstructed circulation being the result of arterial spasm receives confirmation from the fact that very similar phenomena result from a demonstrable mechanical block of the same system of vessels. I refer now to the striking resemblance between the symptoms of cholera-collapse and the results of embolism or thrombosis in the pulmonary artery.

It will be known to most of those whom I have now the honour to address, that for a number of years I have maintained that the impeded circulation through the lungs, which obviously exists during the collapse stage of cholera, is explicable only on the hypothesis of abnormally energetic contraction of the pulmonary arterioles. And I now desire to direct attention to the very striking resemblance between the symptoms of choleraic collapse and those which have been observed in some cases of obstruction of the pulmonary artery by fibrinous clots.

I have references to several cases of pulmonary embolism in which the symptoms bore a more or less striking resemblance to those of the collapse of cholera; but the most complete record of such a case is one which was published by Dr. Alfred Carpenter (*Lancet*, September 23rd, 1871). In that case, as Dr. Carpenter remarks, "the only symptoms wanting to make it apparently one of cholera were alvine discharges and cramps of the limbs". The symptoms actually noted, and which in the choleraic cases have very commonly been supposed to result from the dehydration of the blood by the intestinal discharges, were the following: blueness of the surface; icy coldness of the uncovered parts of the body; cold clammy perspiration; coldness of the breath; sinking of the eyes; feebleness of the voice; a feeble thready pulse; with quick breathing, excessive thirst, and almost complete suppression of urine, two ounces of urine only having been passed one day, and on another day less than two ounces. After death, the right side of the heart was found fully distended with dark-coloured blood, while the left side was empty. The pulmonary artery at its origin was partially obstructed by a clot of fibrinous matter, which sent branches into the ramifications of the artery for several inches; these did not block up the passages entirely, but floated like semi-

cylinders in the current. It is obvious that, if the trunk of the artery and its main branches had been completely obstructed, death must have been as instantaneous as in the case of cardiac thrombosis which I mentioned in the early part of this lecture; and it can scarcely be denied that the symptoms which resulted from this partial obstruction of the arterial trunk bear a striking resemblance to those of choleraic collapse. Such a case, therefore, may fairly be cited as evidence in support of the theory of arterial contraction being the main cause of the impeded pulmonary circulation during the collapse stage of cholera.

Again, it is not without interest to remark upon the very striking resemblance between the symptoms of choleraic collapse and a severe fit of spasmodic asthma. For the purpose of illustrating this, I will take Dr. Hyde Salter's graphic description of the asthmatic paroxysm. He says: "If the bronchial spasm is protracted and intense, the heat of the body falls; the oxygenation of the blood is so imperfectly performed, from the sparing supply of air, that it is inadequate to the maintenance of the normal temperature; the extremities especially get cold and blue and shrink. I have known the whole body deathly cold and resist all efforts to warm it for several hours. But, while the temperature is thus depressed, the perspiration produced by the violent respiratory efforts may be profuse, so that the sufferer is at the same time cold and sweating. It is this union of coldness and sweat, combined with the duskiness and pallor of the skin, that gives to the asthmatic so much the appearance of a dying man. The pulse during severe asthma is always small, and small in proportion to the intensity of the dyspnœa; it is so feeble sometimes that it can hardly be felt." I scarcely need insist upon the many points of resemblance between these symptoms and those of cholera. What, then, is there in common between these two forms of collapse? Obviously not a drain of fluid from the blood, which was at one time looked upon almost universally as the main cause of choleraic collapse; not, I repeat, a drain of fluid from the blood, but a partial arrest of the pulmonary circulation. In both classes of cases, there is evidence of an impeded pulmonary circulation, the result of spasm of the muscular arterioles. In cholera, the arterial contraction is a primary result of the irritant action of the poisoned blood upon the vessels and the vaso-motor nerves; while in asthma the arterial spasm is a secondary result of a partial apnœa occasioned by primary spasm of the bronchi. Using the words asphyxia and apnœa in their strictly literal sense to express pulselessness and

breathlessness, we may say that in cholera-collapse there is a primary asphyxia, and a secondary apnœa consequent on the blood-stasis in the arterioles before it can reach the capillaries to be aërated. On the other hand, in asthma there is a primary apnœa caused by bronchial spasm which cuts off the air from the pulmonary vesicles, and a secondary asphyxia the result of arterial contraction.

In conclusion, Sir, I venture to express a hope that the brief survey which we have taken of some of the pathological phenomena with which the muscular arterioles and the vaso-motor nervous system are intimately and obviously concerned has not been without interest even for this learned audience, to whom I desire to offer my cordial thanks for the attentive hearing with which they have favoured me.