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OF THE

ARTERIES AND VEINS IN BRIGHT'S DISEASE

BY

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A STUDY OF THE ARTERIES AND VEINS IN BRIGHT'S DISEASE.[1]

FOR some time past my clinical observations made annually in the wards of a large general hospital have led me to feel how unsatisfactory is our present understanding of the cause of many forms of heart disease, and of the mode of origin of Bright's disease, and at the same time how difficult it is to arrive at a satisfactory understanding of a case in which these two apparently far apart diseases are, as so commonly happens, coexistent. The intimate relation of disease of the two organs is so well known that for some years medical literature has been filled with various theories to explain how the one is dependent upon or caused by the other. As a result of the observations of Bright it soon became well known that hypertrophy of the heart—and it was said of the left ventricle in particular—was very commonly associated with disease of the kidney; and naturally enough it was thought, as the clinical history of such cases demonstrated the existence of kidney disease long before that of the heart became known, and often the heart disease was not suspected at all before the autopsy was made, that the heart disease was entirely dependent upon, and caused by, that of the kidney, and complicated theories were brought forward to explain how the train was set in motion, and the various steps from its inception to its final development. Soon clinical medicine demonstrated that in many cases in which the coexistence of heart and kidney disease was un-

[1] Read before the College of Physicians of Philadelphia, June 6, 1888.

deniable the history occasionally proved beyond peradventure that heart disease had existed before there was any suspicion, much less evidence, of disorder of the kidney. New theories were required to explain this condition, and they were soon found, principally in the results of congestion of the internal organs, and of the kidneys in particular it was assumed, which was a necessary result of disordered action of the heart. Another step was the observation that the two organs—heart and kidney—are connected by an immense vascular highway, the arterial system, which was found in many instances to partake in the disease; for atheroma of the arteries, more or less extensive, is a common accompaniment of combined heart and kidney disease. Parenthetically it may be observed here that it is curious that comparatively little is to be found in medical literature in regard to the state of the venous system, either in the form of study of its physical condition, or of theory in regard to what might be expected to happen to the veins, though the rest of the subject has been from many points of view somewhat overloaded with theories. This is strange, when it is recollected that the venous highway connecting the two organs is just as large and fully as important as the arterial. The observations of Dr. George Johnson of the hypertrophy of the muscular coat of the arteries of the kidney, and later of the same hypertrophy in various other tissues and organs in cases of red granular contracted kidney, and those of Virchow of the state of the arteries in amyloid disease, constitute important landmarks in the development of our knowledge of the whole subject, and this though there has been, and is, great difference of opinion in regard to the interpretation of the various facts observed. The paper of Gull and Sutton upon the so-called arterio-capillary fibrosis was the first systematic attempt to show that many cases which had previously been called Bright's disease of the kidney were, in truth, due solely to changes which had their origin in the arteries and capillaries, and in the connective tissue in which they lie. This was

a bold step in advance, and has done much toward leading to a clearer comprehension of the complaint by ridding the minds of pathologists of the idea that the disease was Bright's disease of the *kidney*, and that in that organ alone must they dare to seek for the original source of the pathological train. The observations of Gull and Suttor, though of great value in thus clearing the atmosphere of this old doctrine, have not been borne out in other respects by subsequent and more extended observations. Their assertion that the origin of the vascular changes is to be looked for in the adventitia of the arteries and in the capillaries can hardly be considered to have been substantiated. With regard to capillaries our present means for their study are not satisfactory, and little has been even asserted, up to the present time, of their diseases, except that in some cases it has been considered that the walls of the Malpighian tufts of the kidneys were thickened, and again, that there was in various organs increase of the perivascular connective tissue. So far as the first assertion is concerned—that the walls of the Malpighian capillaries are thickened—it cannot be considered as having been proved, though it is exceedingly likely; and for the increase of connective tissue it yet remains to be demonstrated that this is a part of, or even due to, the capillaries, with regard to the real physical condition of the walls of which we are still somewhat in ignorance. No attempt to study the condition of the capillaries in dead tissues, further than to trace their course, has as yet yielded any conclusive results. Nor has it by any means been demonstrated that the changes so extensively found in the arteries and arterioles have their origin in the adventitia.

The present state of knowledge of the complaint seems to be about as follows: It has long been known that in cases of albuminuria certain physical changes take place in the kidney, and that very commonly there is enlargement of the heart, and further, often there is atheroma of the larger arteries, which is more or less extensive as the

case may be. It has, besides, been demonstrated that other changes, chiefly of a degenerative or atrophic nature, are found in many of the various organs and tissues of the body—namely, disease of the cerebral arteries, and of the arteries and substance of the spinal cord,[1] emphysema and slow inflammatory processes in the lungs, calcareous and allied forms of disease of the heart valves, degenerations of the coronary arteries, and fibroid change of the muscular substance, and various forms of disease of the liver and spleen. Such being the case, quite a number of the medical minds that have bestowed attention upon the subject have been struck with the idea, and have enunciated the belief that this hydra-headed disease, or collection of related diseases, as the event may prove it to be, had its origin in the arteries or capillaries, or both, though no one has as yet shown what the mode of origin is; Dr. Johnson, and those of his school, believing it to be one of the so-called blood-diseases which produces its first physical change in the secreting cells of the kidney, while Gull and Sutton, and their following, equally strenuously uphold the opinion that the disease has its origin in the adventitia of the arterioles, and in the capillaries and perivascular connective tissue.

The utter inadequacy of a diagnosis of valvular disease of the heart, or Bright's disease of the kidney, in cases of this nature, as at all descriptive of the real conditions, has pushed itself upon me so forcibly of late years that I have been in the habit of saying, and recording in my clinical histories, that these cases were of vascular origin. Sometimes it seems like the natural result of the advance of years, the machinery wearing out simply because it is too old; or, again, it is as if premature old age came upon the patient, or perhaps he is worn out by dissipation, or because he has earned his livelihood by some physical labor

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[1] Gull and Sutton: On Changes in the Spinal Cord and its Vessels in Arterio-capillary Fibrosis, Trans. Path. Soc., London, vol. xxviii., 1877.

so severe that it necessarily speedily exhausts his vital forces and produces the physical disorganization. The absurdity of the old practice of endeavoring to elicit a history of rheumatism, and then, if the slightest account of joint pains during the past life could be had, of attributing the disease to that, I have long looked upon as the weakest explanation. It is now well known that rheumatism, instead of being, as was formerly thought, almost the sole cause of valvular disease of the heart, is but one of many, all of which are equally capable of producing it. Dr. Allbutt[1] long ago, in an able article, expressed his opinion that, in the large manufacturing town in England in which he lived, heart diseases in hospital practice were much more common among young men as the result of overexertion of the body than of acute rheumatism.

As clinical study has seemed to do little for me in the direction of showing what is the original physical change or pathological basis of the disease, but has merely taught me to be able to predict, with a good deal of accuracy, that, in addition to the well-known lesions in the heart and kidneys, other very widely diffused changes will be found if sought for after death, I have turned from the wards to the post-mortem room in the hope that thus some light might be shed upon the subject. In this way I have been led to the observation of facts which, I trust, may be worthy of the consideration of the profession. It is with a profound sense of the wisdom of Sir James Paget's observation,[2] that "medicine and surgery are eminently a science of observation; deductions from facts are always unsafe; I believe that they have done far more harm than good; and, for the most part, when sufficient facts have been collected and arranged, the general conclusions that may justly be drawn from them are nearly manifest," that I attempt to describe what I have seen. If I should

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[1] The Effects of Overwork and Strain on the Heart and Great Blood-vessels, St. George's Hospital Reports, v., p. 23.

[2] Address at Owen's College, Lancet, October 15, 1887.

be led into making deductions, and few men can resist the inclination, which seems a natural one to thinking beings, the already quoted wise saying must be remembered, and a sharp line drawn between that which is a result of observation and therefore fact, and what is merely theory or deduction.

The first things that strike one who reflects upon this combination of heart and kidney disease is the intimate connection there is between the two organs by the vascular system, the arteries and veins, and that if the disease begins in one organ and extends to the other, this must be the channel of communication ; or that perhaps it does not originate in either, but in the blood-vessels, and secondarily extends to the organs. This latter preconception is rendered still more probable when it is remembered that degenerative changes parallel to those found in the heart and kidneys exist in many other organs and tissues, and it therefore becomes much more easy to believe that the vascular change is the cause and not the consequence. In pathological investigation, therefore, with a view to further elucidation in regard to the original cause, my mind has been occupied with the preconceived idea that the search must be prosecuted by study of the physical conditions of the arteries and veins, and perhaps the capillaries. This statement is made with the knowledge that wherever blood-vessels go they are accompanied by nerves, and that it is possible, and from a purely theoretical stand-point as likely, that the pathological lesions under discussion originate in the nerves as in the blood-vessels. Drs. Da Costa and Longstreth [1] have asserted that in Bright's disease there is a constant lesion of the renal nerve plexus, and have expressed their opinion that this lesion is the cause of the kidney disease, and have further suggested that a similar lesion may exist in other ganglia

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[1] Da Costa and Longstreth : Researches on the State of the Ganglionic Centres in Bright's Disease, American Journal of the Medical Sciences, July, 1880.

producing parallel effects, as, for instance, in the cardiac plexus, causing the hypertrophy of the heart. Though this is of course an explanation which may be correct, it has been by no means proved, and even if extended investigation should show nerve-lesions to be as constant a feature as are the blood-vessel changes, it remains to be discovered which, if either, is the real original cause, for upon purely hypothetical grounds the two are perhaps equally acceptable.[1]

In making somewhat extended post-mortem investigations the lesion I have found to be most constant and most extensively distributed throughout the tissues is disease of the arteries and arterioles, a condition in which, so far as my observations have carried me up to the present time, though I confess that the study has not as yet been exhaustive, the veins seem to participate. In regard to the condition of the capillaries I have nothing to say, for, as already stated, there is no known satisfactory method of studying their physical condition in dead tissues. It is a commonly recognized fact that in cases of the so-called Bright's disease there is ordinarily present a greater or less amount of atheroma of the larger arteries; and Johnson upon the one hand, and Gull and Sutton on the other, and when these names are mentioned it must be understood that all other observers who have either preceded or followed them in the same lines of investigation are included, have made extensive observations in regard to the state of the minute arteries in many of the organs and tissues of the body. Their conclusions have been quite different from those reached by me, though in the course of my investigations I have fallen upon appearances

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[1] Since the above was written Dr. Da Costa has published another paper upon this subject, giving the results of microscopic examination of the cardiac ganglia in cases of Bright's disease, and announcing that extensive organic changes were found—The Middleton Goldsmith Lecture on the Relation of the Diseases of the Kidney, especially the Bright's Diseases, to Diseases of the Heart—Medical News, May 5, 1888.

similar to those they have described. I have made sections from the brain, spinal cord, lungs, heart, liver, spleen, kidneys, and of various of the larger arteries and veins, and in all of them—except the spinal cord, and with regard to its condition my examinations have not been sufficiently numerous to be conclusive—have found quite constantly present an irregular overgrowth and thickening of the intima of the arterioles. This thickening varies very much in its anatomical characters and its extent, and often when it is present in high degree there is involvement of the other coatings, though ordinarily they have undergone no change. The morbid appearances will be better understood from an examination of the plates than would be possible from any written description. The condition appears to be nothing but that which is described in text-books of pathology as the various forms and stages of atheromatous change, but observers do not seem to have connected its existence with this disease further than to have noted that it was commonly present in the larger arteries. The appearances found differ much in accordance with the size of the vessel in which they are observed, and in different organs. In larger-sized vessels the more commonly understood atheromatous changes will most usually be found—misshapen vessels, calcareous deposits, loss of substance of intima, thickened patches upon the inner surface (these being often so extensive as to cause great obstruction to the blood-current, sometimes the lumen of the vessel being a mere chink at one side; see plate, Fig. 5), and where the condition has progressed to its full development, more or less destruction or alteration of the entire thickness of the walls. In smaller ones the changes are most commonly confined to increased thickness of the intima, which is not usually so irregular in degree at different portions of the circle as is the case in large arteries, though it is seldom absolutely uniform. The intima in such vessels, when examined in cross section, often has a thickness which will be half as great as, or even equal to, that of the muscular coat, but it may

vary to almost any extent. This tissue, when examined under the microscope, appears to be composed of fibrous material, the fibres of which, when the vessel is viewed in cross section, appear to be circular, and in longitudinal sections to run lengthwise ; there are, therefore, probably abundant fibres running in all directions, thus giving the tissue considerable strength. Contrary to what is commonly stated, I have usually found this morbid tissue to contain here and there numerous nuclear elements. In the larger vessels in particular, and where the patches of atheromatous thickening are large, they are often composed of a well-organized tissue containing numerous cells, which in their appearance and arrangement resemble granulative tissue, seeming disposed to arrange themselves in nests, as is common in young and rapidly growing tissues.

The well-organized cellular outgrowth of the intima in these cases is identical with that which has been most frequently described as syphilitic endarteritis, and yet I have seen it in a number of cases in which there was neither a history of syphilis nor reason to suspect the existence of that disease. Examination of the endocardium and valves of the left heart often shows a condition precisely parallel to, and seemingly a part of, the same process, the evidences of which exist so extensively in the arteries. It seems positive that the endocardial and endarterial changes are but part of the same disease, and that this is the cause of the valvular changes which so frequently arise, complicating the trouble, and, when they exist, much hastening the inevitably fatal result. In examining the thickened patches of endocardium, and in sections of aortic valve flaps, thickened and distorted by the disease, there were found the same nest-like arrangements of cells described as existing in the intima of the arteries.

While the above-described conditions are those I have usually seen as a result of examination of the arteries, I have not, as a common thing, found the increased thickness of the muscular coat which is described by Johnson, and called by him a hypertrophy, to be present in such

degree as to render its existence undoubted. Arteries may often be found in which it could be said that the middle coat was unduly thick, and, again, others, in regard to the state of which there might be dispute, but in most instances I have failed to find an increase so great that its existence could be considered to be beyond doubt. It is a much easier matter to be sure that the appearances described of the intima are morbid; for, in the natural state, in small vessels certainly, it constitutes but a very thin layer, and besides, when it is seen to be many times thicker, as happens in many instances, upon one side of transverse section of an artery than upon the other, there cannot be a shadow of doubt that such an appearance is pathological. This is very different from what is found in regard to the muscular coat, which, if at all thickened by disease, is uniformly so, and there is, therefore, nothing to contrast it with, and its state can be merely estimated as a matter of judgment. It is curious that in one case in which I made many sections (case of J. K——) of different organs and vessels, the only artery in which there was undoubted thickening of the muscular layer was one of the primary branches of the renal. In this vessel the intima was thickened to a slight degree, but much more so at some parts of the circle than at others, and the plicated membrane very distinctly visible around the entire circuit; the muscular coat, however, which was probably of twice the ordinary thickness in a vessel of such size, did not present the appearances which could be called those of true hypertrophy; for, although the muscle bands and nuclei were present and numerous, there were also visible very many other cells which were exactly like those described as so commonly found in the overgrown intima. These cells were, so to speak, wedged in between the muscle elements, and many of them were undergoing pigmentary degeneration. Sections of the abdominal aorta in this case, and of the minute arterioles in the renal substance itself, did not show any indisputable increase of the muscular coat, though there was in both overgrowth of the intima. To

anyone who would wish to advocate Dr. Johnson's view, that increased thickness of the muscular layer is a true hypertrophy, and that it increases what he calls the "stop-cock" power of the arterioles, does it not seem strange that the only artery that showed undoubted increased thickness of the middle layer in this case should, in that very layer, present the marked evidences of a degenerative process, and that the vessel affected should be a very large one, to which, ordinarily, is attributed elasticity and not much contractility, while the minute arterioles of the kidney, the very citadel of the supposed condition, should present none of it, and all the vessels in the neighborhood should have plainly thickened intimas?

Fig. 9 represents two views of a minute artery removed from a kidney under a dissecting microscope. The upper one is intended to produce the same effect as Johnson's ("Medical Lectures and Essays," by George Johnson, 1887) picture, from the appearances of which he makes his assertion of the existence of hypertrophy of the muscular coat. The vessel was carefully dissected out, then split open with scissors, and mounted with the inner side up, thus showing half of the internal surface of the vessel and the thickness of its walls at the cut edges. No fibrous coat is distinguishable, and the same holds good in Johnson's figures, but the muscular coat and intima are very well shown. Whether the muscular coat is increased or not I think might well be disputed, as this layer in the walls of an artery of such size is always a marked feature in a picture; that the intima is increased in amount, and, as represented in the picture, irregularly so, there can be no doubt, though it might be said that this is due to the crude method of preparing the object, to dissect it out and then cut it with scissors. That such is not the case, however, and that the intima is actually thickened, and irregularly so, is made very plain by the other picture. This is a bit of the same artery, and the section was prepared by cutting off from the end, before it was split open, as thin a section as could be made with a pair of scissors,

and it very well shows the thickened intima lying within the plicated membrane, which latter is not distinguishable at all in the longitudinal section. To my mind it becomes evident from the contrast presented in these two pictures that the change of the intima is a much more positive and unmistakable one, and one which in the nature of things is capable of producing quite as grave effects as that of the muscular coat, upon the existence of which in this vessel doubt may be cast; a change also which, even if in other vessels its existence is undeniable, is accompanied by degenerative processes so extensive as to render its proper classification as a true hypertrophy uncertain.

So far as the "fibrosis and hyaline-fibroid" condition described by Gull and Sutton is concerned, I have failed to discover it in its full development. They declare their belief, and try to prove, that the vascular changes have their origin in the fibrous coat, and describe a high degree of thickening of the adventitia as being usually present. There can be no doubt that there is great increase of fibrous tissue, and it is found more extensively developed around the blood-vessels, the place in which connective tissue exists more abundantly than elsewhere in all organs; but its appearances are more those of a general increase of perivascular connective tissue than of the adventitia of arterioles alone. And for the matter of that, how is it possible to decide, in any section examined with the microscope, where the fibrous material lying outside the muscular coat of an artery ceases to be adventitia and becomes perivascular connective tissue? The two structures are identical and shade into each other without any defined boundary. Nothing that answered the description of hyaline-fibroid change of arterioles has come under my notice except certain appearances presented by the vessels in sections of the spinal cord; in the thoracic and abdominal viscera I have failed to find it, and cannot comprehend why this should be unless it is, as stated by Johnson ("Medico-chirurgical Transactions," vol. lvi.), that their methods were faulty and that the use of glycerine and

camphor in mounting produced the appearances described. In the spinal cord I have found arteries with walls that looked entirely structureless except for a few nuclei lying at the edge of the lumen of the vessel, and answered exactly to the appearances described and figured by Gull and Sutton ("London Path. Soc. Trans.," *loc. cit.*). It might be well to mention here, as a matter of interest, though I have no explanation to offer, and do not know if it had any bearing upon the condition, that in this same case, which was one of marked Bright's disease, the olivary body, and nucleus dentatus within it upon the right side, was much larger than the left, though no morbid condition of the tissue itself could be discovered upon either side.

In two cases in which I made extensive microscopic examination of the tissues, and they are the two from which the vessels represented in the plates were taken, I found morbid changes in the veins as well as the arteries. Atheroma of veins so extensive as that of the femoral, which is shown in Figs. 7 and 8, is not usually described as being common, though the occasional occurrence of the disease in veins is sufficiently well known. After the section from which the picture is made was prepared, it was found impossible to determine with certainty, from the microscopic appearances alone, that the larger vessel of the two was really a vein, so great is the thickening of the intima and fibrous coats, and it was only by a careful examination of the piece of tissue from which the section was cut, and the discovery of a well-marked valve in the vein, that an absolute conclusion was reached. The two vessels, which were removed from the upper part of the thigh together, were found to be rigid, like bony tubes, and it was only after decalcification that sections of them could be cut. The process of disease in this vein appears to have been exactly the same as takes place in arteries, some thickening of all the coats, perhaps, for when considering the state of the muscular layer it must be remembered how thin it is in a natural condition in veins, and of the intima in particular. It is a noticeable fact

that the thickening of the intima varies very much at different parts of the circle of the vessel, in this respect being precisely parallel to what has already been so much emphasized as occurring in arteries. The structure of the intima also appears to be similar in character to that found in arteries. How the two inner coats became loosened from the fibrous one, as appears in the plate, cannot of course be known; but it may be that the breakage occurred in removing the vessels from their position in the thigh, for so rigid were they that it required the exercise of some force to remove them.

Fig. 12 represents a portion of a vein lying in the adipose tissue covering the front of the heart, and presents a condition of which I have never seen any description. In most of it the walls are very thin and the tissue of a very loose texture, but in the intima there are two spots opposite each other in which marked cellular outgrowth has taken place and the cells have in the most distinct way arranged themselves in nests precisely like those described as existing in the arterial system. When this is examined with a higher power the arrangement of the cells can be still more plainly distinguished.

In most of the veins I have examined in this disease, what has struck me most forcibly in them has been the tenuity of their walls and the looseness of texture of the material of which they were formed. This can be seen to some extent with the naked eye as well as by the aid of the microscope. I have found that it is not uncommon, if a vein is cut open, spread out flat, and then held up to a strong light, for the walls to vary much in thickness at different parts, and in some places to be exceedingly thin. In the case of J. K——, sections were made transversely across a large branch of the renal vein, and the walls were found to be so thin that it seemed astonishing how it could have been at all an adequate container of blood.

In regard to the structural condition of the capillaries, for reasons already mentioned I do not even pretend to an opinion.

It may perhaps now be permissible to attempt to draw some contrast of the general features of the two cases from which my illustrations were taken. That of J. K—— was made the subject of a short paper read before the Philadelphia Pathological Society in the early part of 1888, and published in the "American Journal of the Medical Sciences" for June of the same year, and it will therefore not be well to do more than sketch the outlines of the case again. It was one of typical aortic regurgitation in a man fifty-four years of age. The heart disease came on late in life and without the occurrence of any attack of rheumatism more than some vague joint pains, which never confined him to bed, and he died gradually of heart failure, without dropsy or anything to point to involvement of the kidneys, except that when he first came under notice there was a trace of albumen in the urine, without casts, which, however, soon disappeared never to return. After death there were found brown atrophy of the heart, fibroid degeneration, thickening of the endocardium and of the aortic valves, and in both of these the existence of the peculiar cell-growth which has been described. The arteries and veins of the heart presented appearances already mentioned (Figs. 11 and 12). The lungs gave evidence of some catarrhal inflammation and their arteries of thickening of the intima. The liver-cells were much degenerated, and the arteries as in the other organs. The kidneys exhibited evidence of parenchymatous disease, there were casts in the tubules, and the arteries showed the same change as found in vessels elsewhere (Figs. 9 and 10). The condition of the renal artery and vein, and of the abdominal aorta, vena cava, and a small branch of the cava have already been mentioned. There were large inflammatory bands in one of the iliac veins, causing obstruction in that vessel.

The case of J. C—— presented in many respects a contrast. He was fifty-one years of age, and had suffered with some shortness of breath and palpitation for three years. When admitted to the hospital, about two months before his

death, there was great dyspnœa, amounting to orthopnœa, and of this he never got rid. Dropsy and difficulty of breathing increased, and his sufferings became worse and worse; nothing seeming to afford him any relief until, finally, he died, having suffered what was almost agony. The conditions were in all respects those usually regarded as typical of Bright's disease, except that no casts were found in the urine, though albumen was always present. Post-mortem examination showed that the heart and all its openings were much enlarged, there was extensive brown atrophy of the muscular substance and calcareous deposit in the base of the aorta and valve-flaps. The minute veins exhibited irregular thickening of the intima, and the condition of one of the arterial branches is shown in Fig. 5. The pleura was thickened and the lungs adherent; there was emphysema and some catarrhal infiltration, and the condition of a minute arteriole is represented in Fig. 3. The liver was in a state of fatty and granular degeneration, and the hepatic arteries and portal veins were much thickened and diseased. There had been inflammation around the spleen, binding it to the surrounding organs, and on section it showed marked fibrosis, and the arteries were much thickened, the intima markedly so. There was parenchymatous disease of the kidneys, the capsules were thickened, and there were infarctions, and the arteries diseased (Fig. 4). The radial artery and femoral artery and vein were atheromatous and calcified (Figs. 6, 7, and 8). The abdominal aorta presented distinct irregular thickening of its intima. In the spinal cord there seemed to be some degeneration of the nerve-fibres, particularly of the peripheral nerves, and the arterioles presented the characters described and figured by Gull and Sutton ("London Path. Soc. Trans.," *loc. cit.*) as hyaline-fibroid degeneration. The walls were composed of a material which under the microscope appeared structureless, except that a few nuclei lay at the inner edge. In the medulla oblongata, as already mentioned, the right olivary body and its contained nucleus dentatus was much larger than the

left. The large artery running along the front and that upon the posterior surface both presented in marked degree the irregular thickening of the intima. Figs. 1 and 2 show the condition of the intima of one of the middle cerebral arteries. Sections of this vessel higher up, or rather of its branches after it had divided into three, exhibited irregularly thickened intima in two of them, while the third presented an appearance quite natural.

In these two cases the mode of death and the picture presented by the history of the last few years of life were as dissimilar as could well be, though in many respects the pathological lesions found were singularly parallel. Though in the first case the man died what would commonly be considered a typical heart death, and in the second an equally typical kidney death, and there should have been, reasoning from analogy, a great difference in the pathological lesions, such was not the case. It would be difficult, if not impossible, for anyone, from a study of the pathological lesions alone in these two cases, to say that the modes of death would have been in anywise different. The most important of these lesions, perhaps, were the changes in the heart and kidneys, and in respect of these the two cases were not materially unlike, and in both were found besides extensive changes in the arterial and venous systems, which, though presenting many points of difference, were yet only varying features of what seems to be primarily the same disease.

The disease seems to be very wide-spread in its early effects even, and may first reveal itself clinically by a cough if it takes possession first of the lungs, or by the symptoms of apoplexy, if the brain arteries are the earliest to suffer injury, or by epistaxis perhaps, which has always seemed to me to betoken just as positively a physical change of the arterioles of the nares, though of this there is no pathological evidence as yet, as does the apoplexy show that the brain-arteries are diseased. Often have I found, by the most careful inquiry into the clinical history in cases of typical Bright's disease, that the first

symptom with which the patient has suffered has been cough, and it is a fact well known how often persons dying of apoplexy are found to have had Bright's disease, and it is equally well known how often epistaxis is the first warning given of the existence of kidney trouble. There is, however, no reason, except that Bright first drew attention to the existence of changes in the kidneys (and this is no reason at all), to suppose that the diversified lesions were all caused by the changes in either the secreting substance or in the arteries of the kidneys.

The fact that cerebral hemorrhage and epistaxis are such common accompaniments or symptoms of chronic Bright's disease seems to me the strongest proof that it should not properly be considered to be one of the kidney, for there exists at the present time no evidence to show that the kidney disease which sometimes, but not always, exists in such cases, originated before the blood-vessel change which was their direct cause, nor is there even a very plausible theory to strengthen such a hypothesis.

In conclusion, it may be stated that my desire has been to make clear, by language and pictures, the view that in the so-called chronic Bright's disease, we have to deal with one which is wide-spread in its effects; that the most characteristic and probably most important changes, so far as at present known, are those of the intima of the arteries, in which probably the veins always participate; that changes in the muscular coat and adventitia, though often present, are by no means so important in their effects, and probably are secondary to those of the intima; that the process seems to be coextensive with, and probably is a part of, the change in the large arteries which is so common and so well known as atheroma; and finally, that it seems likely, in the absence of proof that changes in the nerve-substance are a necessary accompaniment, or even if such were proved to be the case, the lack of knowledge that they antedated the disease of the blood-vessels, that the earliest of the now known pathological

lesions to make its appearance is the change in the intima of the blood-vessels.

My paper must not be closed without an acknowledgment of my great indebtedness to Dr. B. A. Randall for the beautiful illustrations I have been enabled, through his skill, to present.

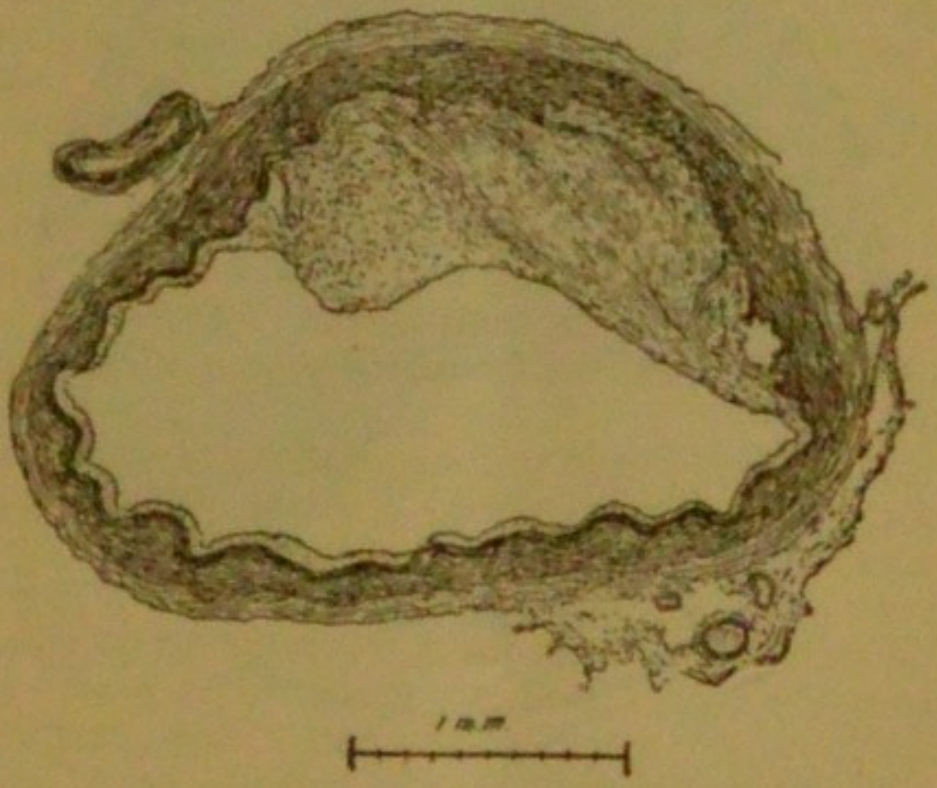


FIG. 1.—Case of J. C——. Middle cerebral artery, showing irregular outgrowth of intima. The accompanying vessels are somewhat enlarged; the adventitia and muscular coats are normal. The plicated membrane shows very distinctly around the entire circle. The intima is seen within the plicated membrane, and is thickened in the entire circuit; but at one side, and occupying about one-third of the circumference, the thickness is very great. At one portion of this mass there are numerous blood-corpuscles, entangled in the tissue, while at another there is distinct cellular structure. × 20 diameters.

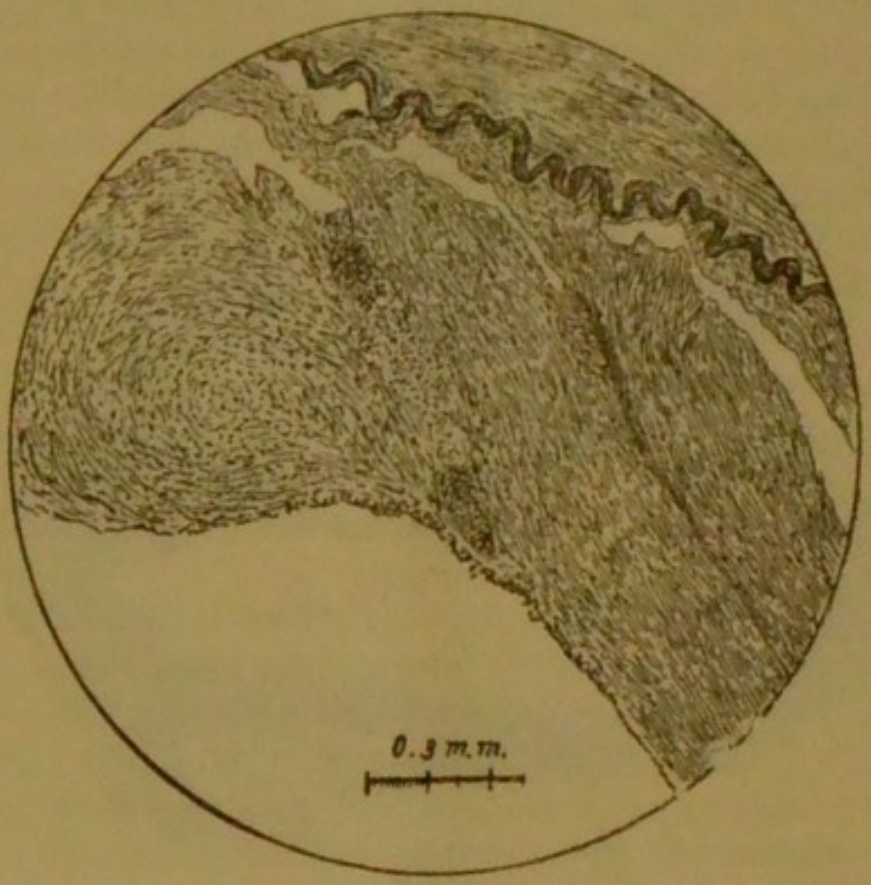


FIG. 2.—A portion of the same artery as Fig. 1, and showing the cell-growth and entangled blood-corpuscles, and that the general character of the structure of the most thickened portion of the intima is a fibrous material. The open spaces are probably due to tearing of the tissue in mounting. ×35 diameters.

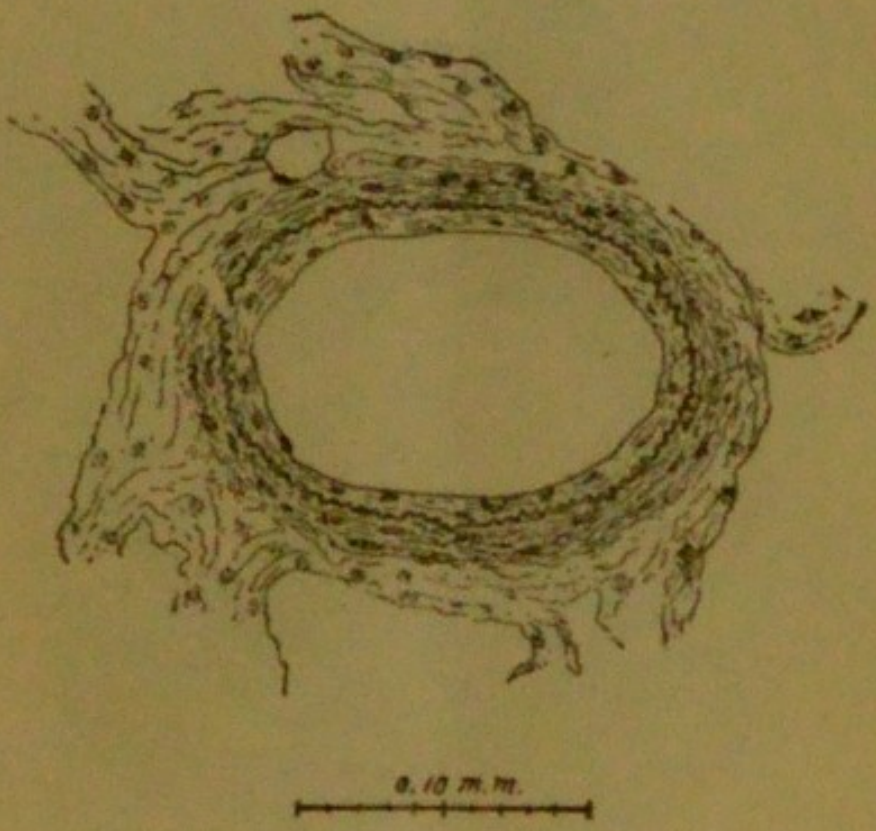


FIG. 3.—Case of J. C——. Minute arteriole from lung, showing great thickening of the intima, which contains a few scattered cells, though most of it consists of a homogeneous, structureless-looking material, quite different from the appearances seen in Figs. 1 and 2. The muscular coat and adventitia cannot be very satisfactorily differentiated, but they do not appear to be at all thickened. The plicated membrane is a marked feature of the picture. × 220 diameters.

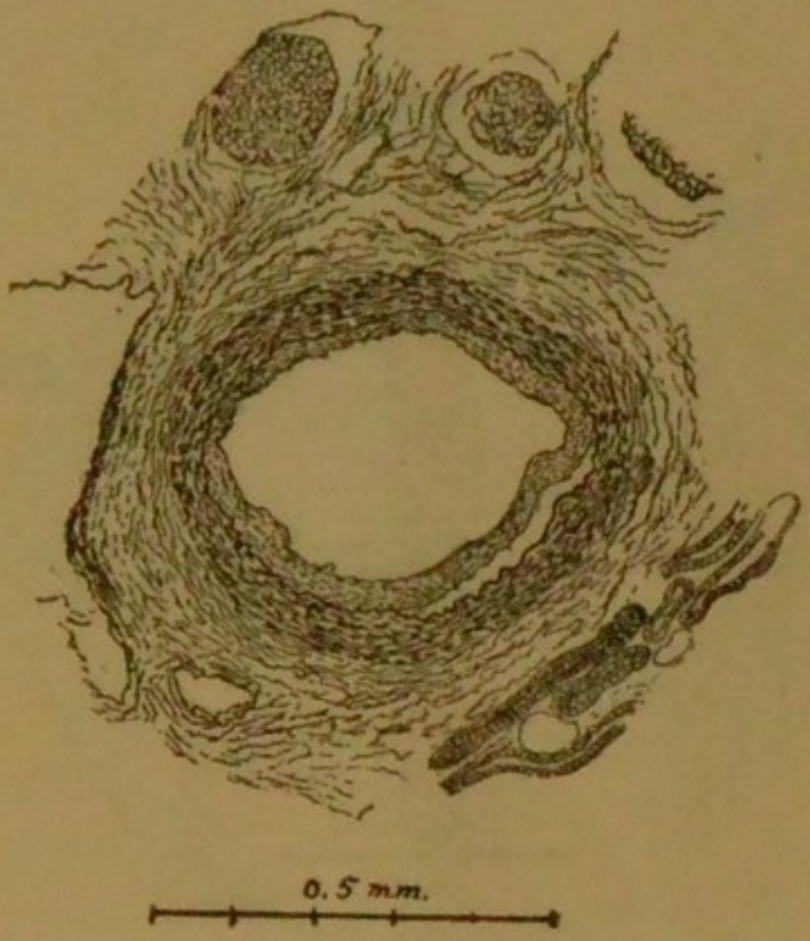


FIG. 4.—Case of J. C——. Minute arteriole from the kidney, showing great thickening of t e intima, which is almost structureless, containing only a few scattered cells; there being in addition merely a few fibres running around the circle of the vessel. × 60 diameters.

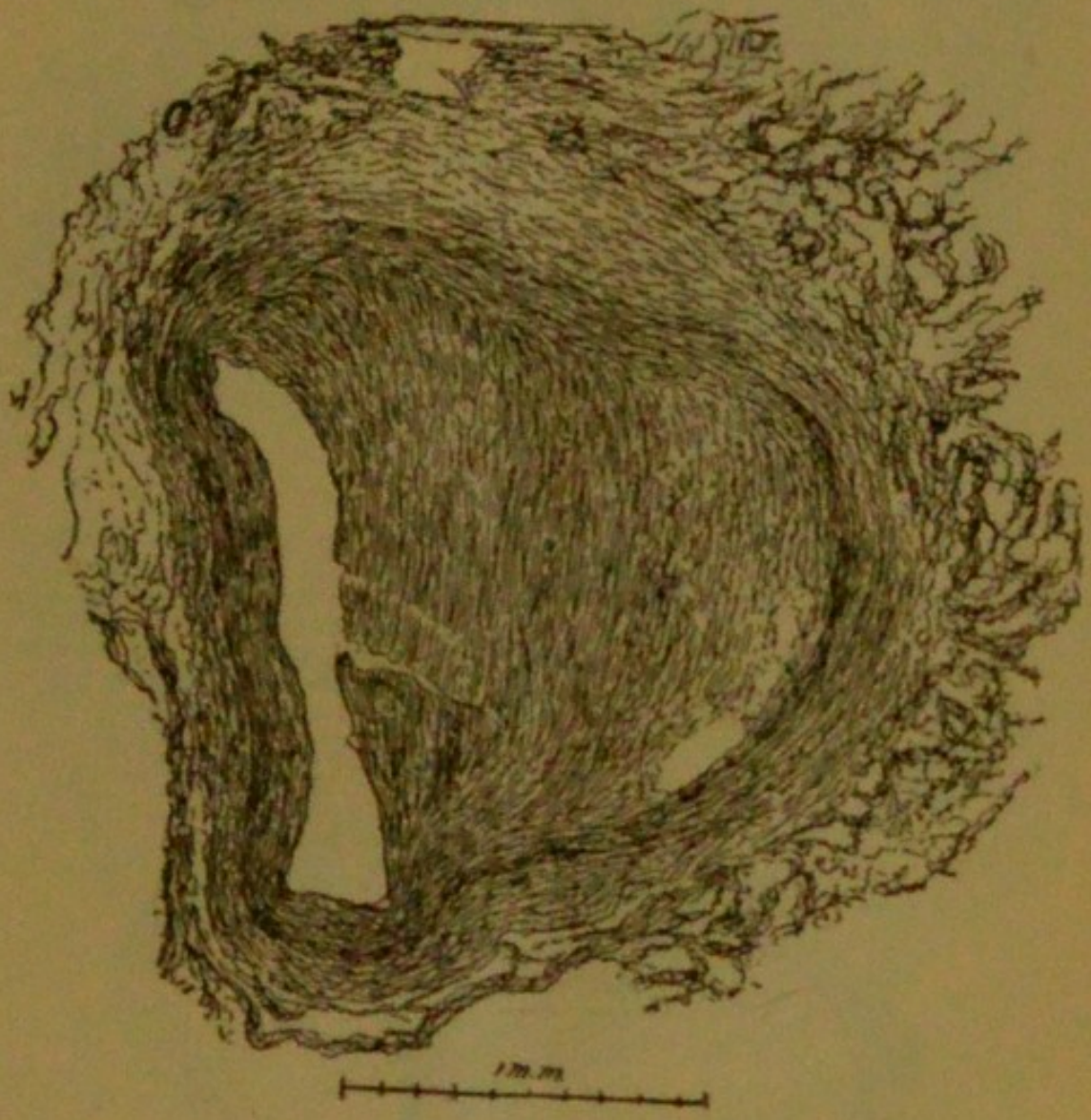


FIG. 5.—Case of J. C——. Branch of coronary artery from anterior surface of heart, showing almost the entire lumen of the vessel filled with an outgrowth, the opening being a mere chink. When seen with the amplifying power used in making the picture, this morbid material has, as represented, merely a fibrous appearance; more magnified, the deposit is seen to contain a great many cells and to be a well-organized fibrous growth. ×28 diameters.

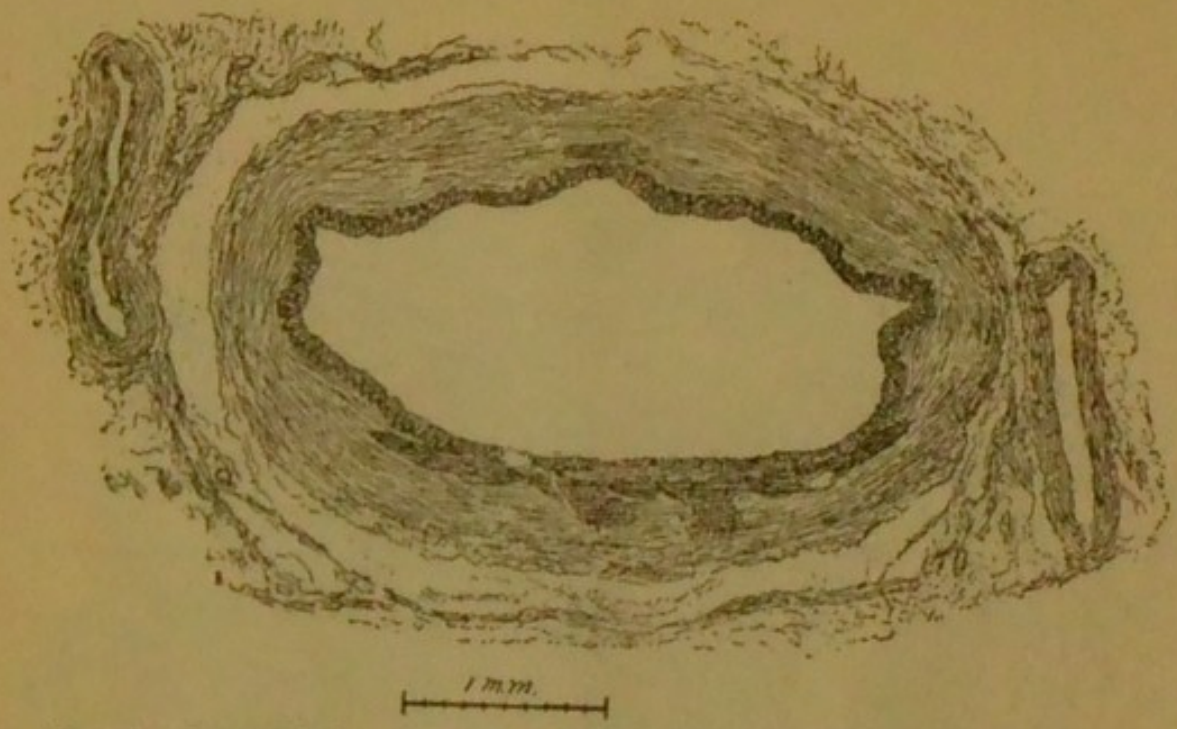


FIG. 6.—Case of J. C——. Radial with two accompanying arteries. It was so much hardened by mineral deposit that it had to be decalcified before sections could be cut. The differentiation of fibrous and muscular coats does not show well, perhaps owing to the soaking in acid to remove the salts, but more likely to the extensive atheromatous degeneration. The plicated membrane is a marked feature around the entire circuit, and the intima within it is much thickened. The atheromatous degeneration has extended deeply into the muscular layer. × 15 diameters.

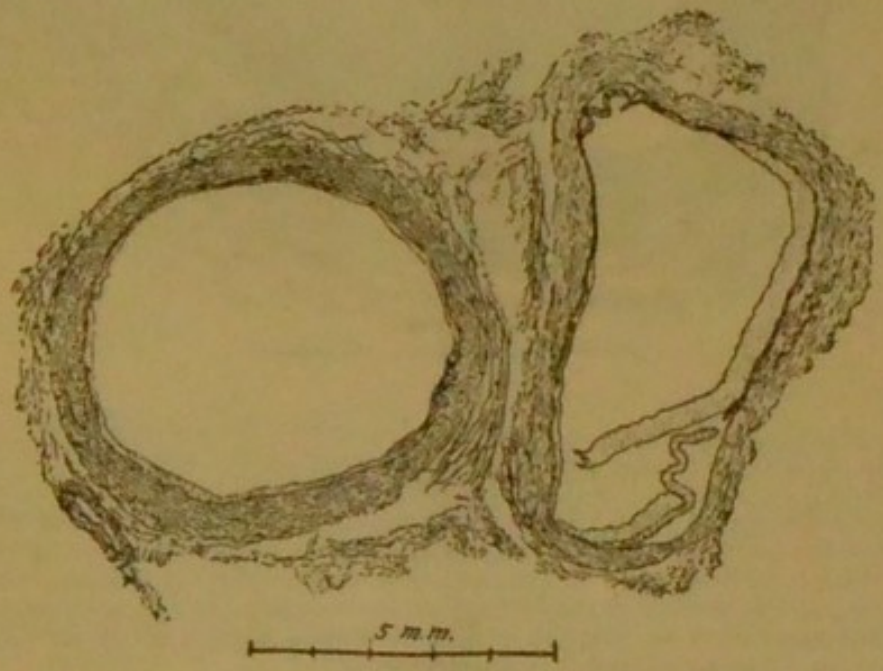


FIG. 7.—Case of J. C —. Femoral artery and vein. Both vessels were converted into rigid bony tubes by calcareous deposit and had to be treated with acid for its removal before sections could be cut. The artery shows ordinary atheromatous changes, the intima being irregularly thickened and spots of degeneration existing in the muscular coat. The vein shows an intima very greatly and irregularly thickened. At one place this coat and the muscular layer are broken loose from the adventitia. This probably occurred in removing the vessels from the thigh, for they were so rigid and firmly fixed in their position that some violence was necessarily used in cutting and tearing them loose. × 5 diameters.

FIG. 8.—One-half of same vein as in Fig. 7, more highly magnified, and therefore better exhibiting the minute structure. × 22 diameters.

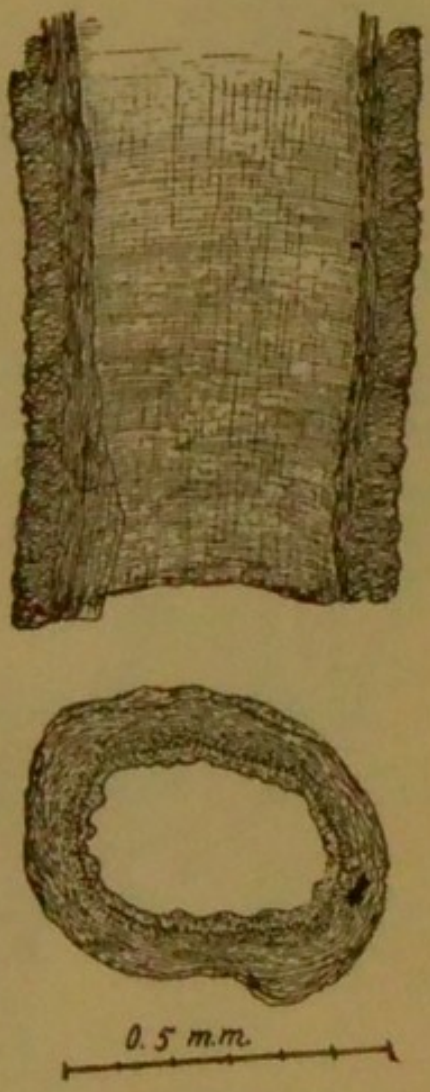


FIG. 9.—Case of J. K——. Views in longitudinal and transverse section of an artery from the kidney, which was removed under a dissecting microscope, and then split in half with scissors lengthwise, and mounted with the inner side upward in imitation of Dr. Johnson's pictures ("Medical Lectures and Essays," by George Johnson, 1887). There are visible the inner surface of the artery and the edge of the intima and muscular coats. The fibrous coat does not show at all, and this is the case in Johnson's figures also. The intima is thickened, and in various degrees at different areas; this might be said to be due to irregular cutting of the vessel, but is disproved by what is seen in the transverse section. The circular view is of the same vessel, but cut transversely with a pair of scissors. This shows marked thickening of the intima and its irregular distribution, and the plicated membrane is a marked feature of the picture, though not visible at all in the longitudinal section. The question whether the muscular layer was thickened in this vessel is one which might well be disputed, though there can be no doubt of the thickening of the intima and its difference in degree at different positions. × 68 diameters.

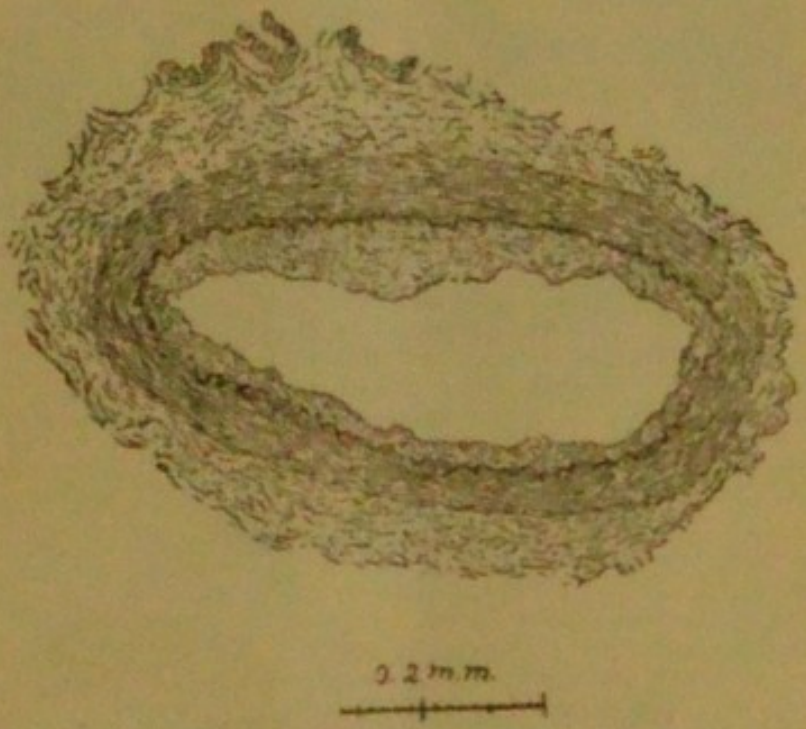
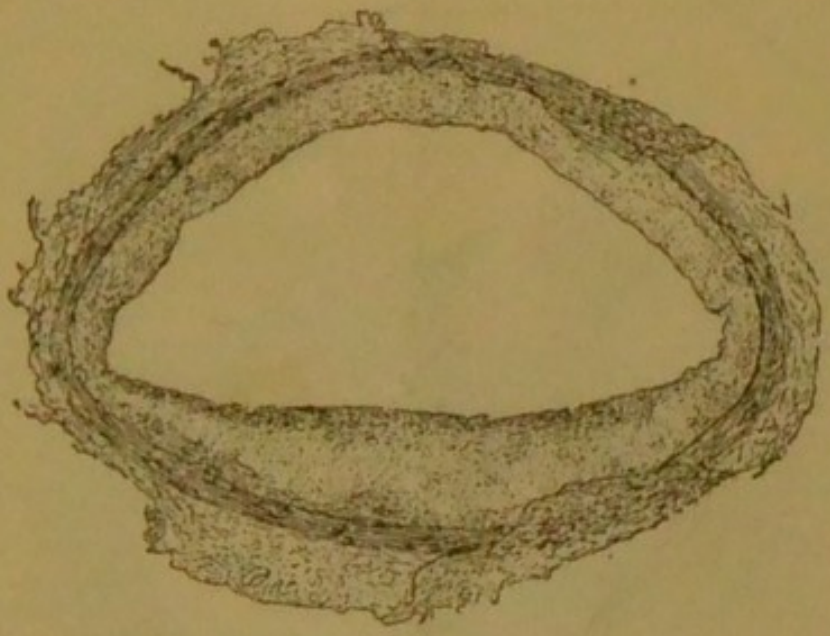


FIG. 10.—Case of J. K——. Minute arteriole from the kidney, showing marked irregular increased thickness of the intima. × 100 diameters.



1. mm.

FIG. 11.—Case of J. K——. Third descending branch of left coronary artery (runs down front of heart in or near interventricular septum), exhibiting, most beautifully, extensive atheromatous degeneration. In two positions there is slight imperfection in the mounting, the outer portions of the section being folded over. There was no calcareous matter deposited in this vessel. The fibrous and muscular coats exhibit no extensive changes, there being merely slight invasion of the latter by the degenerative processes, and this is visible in the lower portions of the figure. The plicated membrane has been destroyed everywhere except in the portion of the artery figured at the right-hand side of the picture, and there it forms a marked boundary between the muscular coat and intima, which latter, throughout its entire area, is most markedly and irregularly thickened. In the lower part of the picture, at the junction of the intima and muscular coats, atheromatous degeneration and softening is shown to have taken place, and extended into both the layers. The state of the intima of this vessel is typically characteristic of the diseased condition which it has been desired to describe and represent. × 12 diameters.

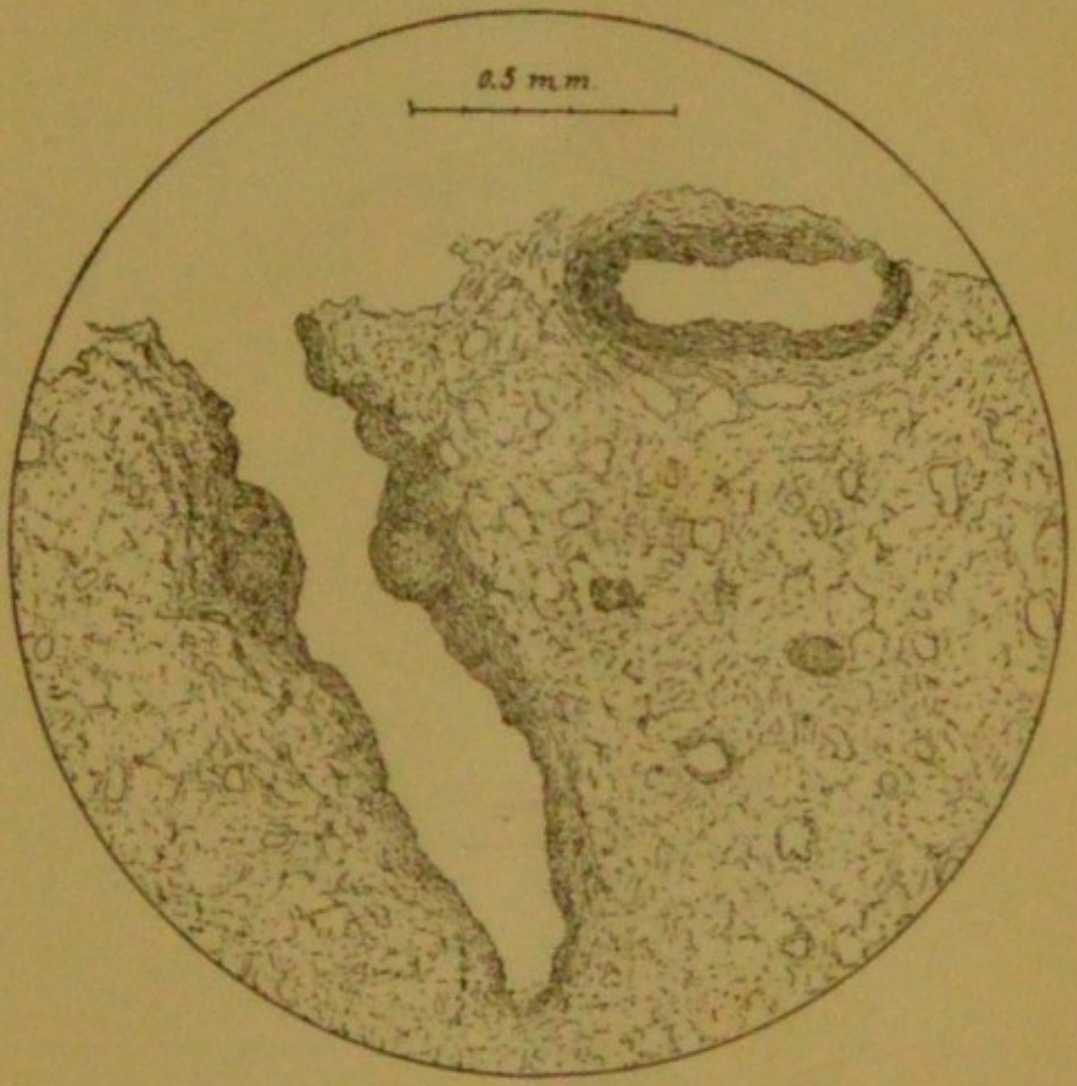


FIG. 12.—Case of J. K——. Of a vein and artery, contained in the adipose tissue, from the anterior surface of the heart, near the interventricular septum. The walls of the vein are generally thin and of loose texture, but there are two masses lying in the intima upon opposite sides of the vessel which are made up of tissue which evidently has a cell-like arrangement. More magnified, this is plainly seen to be composed of cells arranged in nests, and is precisely similar in structure to what is found in the intima of arteries, and in the endocardium and heart-valves. × 40 diameters.

NOTE.—These are from pen-drawings by Dr. B. A. Randall, and the plates were made by photographic process, and reduced from the original size by about one-quarter to one-half.