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The Pathology of the Contracted Granular Kidney

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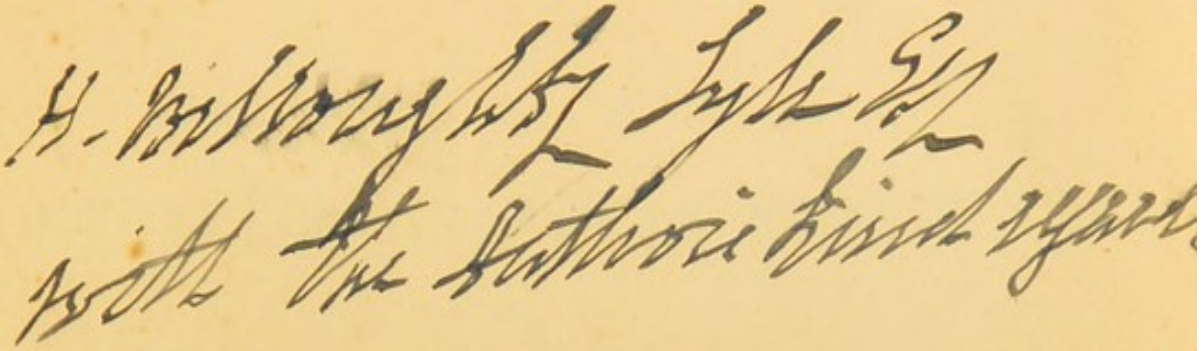

THE PATHOLOGY OF THE CONTRACTED GRANULAR KIDNEY

BY THE SAME AUTHOR

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J. & A. CHURCHILL.

THE PATHOLOGY OF THE
CONTRACTED GRANULAR KIDNEY
AND THE
ASSOCIATED CARDIO-ARTERIAL CHANGES

BY

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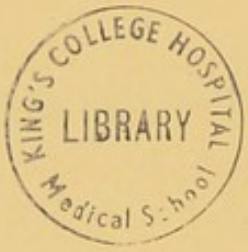
PHYSICIAN EXTRAORDINARY TO HER MAJESTY THE QUEEN

WITH TWENTY-NINE ILLUSTRATIONS

LONDON
J. & A. CHURCHILL
7 GREAT MARLBOROUGH STREET
1896



PREFACE.

The discovery of the structure and function of the arterioles and of the vaso-motor nervous system—the greatest and most important addition to our knowledge of the circulation since the time of Harvey—has thrown an entirely new light upon pathological subjects so entirely diverse and apparently disconnected, as, amongst others, 1st, *Raynaud's disease;* 2nd, the immediate cause of the arrested circulation and death from *apnœa*, badly named *asphyxia;* 3rd, the true nature and proximate cause of the *collapse stage of cholera;* and 4th, the cause of *hypertrophy of the left ventricle of the heart*, which is so frequently associated with the contracted granular kidney. The connecting link between these diverse conditions is the stop-cock action of the muscular-walled arterioles, the systemic arterioles being concerned in the first and fourth of the above-mentioned pathological conditions, and the pulmonary arterioles in the second and third.

In the first part of this treatise I have described and illustrated, more minutely than I believe has hitherto been done, the arterial changes in the granular kidney and throughout the system which

are associated with the cardiac hypertrophy, and I have given what I believe to be the true interpretation of the appearances.

In the second part a renewed attempt is made to show that the wasting of the granular kidney is the result of pathological changes which are primarily and essentially *intratubular*, and that the term *atrophic granular kidney* more truly indicates the nature of the renal disease than *interstitial nephritis*, since there is reason to believe that the pathological process is neither primarily interstitial nor of the nature of inflammation.

If I do not succeed in convincing the supporters of the interstitial hypothesis that their interpretation of the phenomena is erroneous, they will, I trust, do me the justice to admit that the objections to their doctrines are neither unreasonable nor undeserving of serious consideration.

My friends Dr. Halliburton and Dr. Tirard have done me the favour to read the proof-sheets, and in so doing to correct errors which had escaped my observation.

To Dr. Halliburton I am also under great obligation for assistance of various kinds which, in the midst of numerous pressing occupations, he has on many occasions cheerfully rendered me.

11 Savile Row
May 1896

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THE

PATHOLOGY OF THE CONTRACTED GRANULAR KIDNEY.

PART I.

THE CARDIO-ARTERIAL CHANGES ASSOCIATED WITH THE CONTRACTED GRANULAR KIDNEY.

Section I. History of the Discovery of Hypertrophy of the Walls of the Renal and other Systemic Arterioles.

A REFERENCE to various treatises on Pathology and the Practice of Medicine which have been published during the last quarter of a century, will show an embarrassing conflict of statement and opinion as to the nature of the thickening of the walls of the minute arteries in cases of chronic Bright's Disease. In the hope of removing some sources of this confusion and thus facilitating the formation of a correct opinion upon an interesting and important subject, I propose to give a brief history of the successive steps by which our present knowledge of the cardio-arterial

changes in Bright's Disease has been arrived at. In giving this history it will be necessary to indicate some errors of observation and of inference which have been sources of contradictory and perplexing statements.

It is, I believe, generally admitted that the first published account of the thickening of the minute renal arteries in cases of chronic Bright's Disease is contained in a paper of my own in the 33rd volume of the *Transactions of the Royal Medical and Chirurgical Society* published in 1850.

FIG. 1.—NORMAL ARTERY FROM THE KIDNEY.—× 200.

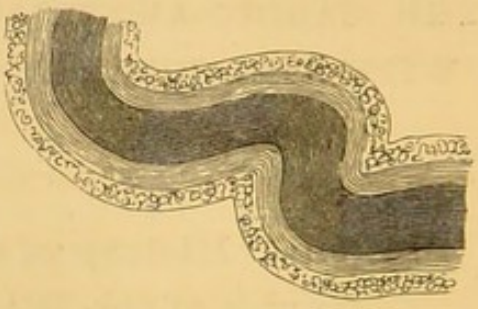

FIG. 2.—ARTERY, WITH HYPERTROPHIED WALLS, FROM A GRANULAR KIDNEY.

An inner longitudinal and an outer circular layer of fibres, of about equal thickness. The canal is injected.—× 200.

Figs. 1 and 2 are exact reproductions of the illustrations contained in that paper. At that time and long afterwards, I believed that not only was the outer circular layer of fibres muscular, but the inner longitudinal layer also.* I supposed the thickening of both layers to be a result of hypertrophy of muscular tissue; and the explanation which I suggested was

* The nature of the inner longitudinal layer will presently be explained.

that in consequence of destruction of the renal gland cells with resulting atrophy of the tubes and impeded circulation through the intertubular capillaries, the arterioles by their forcible contraction assisted the heart to drive the blood onwards, and that their continued over-action resulted in hypertrophy of their muscular walls. The excuse for this erroneous physiology is that it was published about two years before the earliest experiments of Bernard, Brown-Séquard and others had revealed the fact that the function of the arterioles is not to propel the blood, but, by their contraction and relaxation under vaso-motor nerve influence, to regulate the blood supply to the capillaries. This action of the arterioles I afterwards ventured to designate their *stop-cock* function.

The result of more extended observations upon this subject, carried on during a period of seventeen years, is recorded in a paper of mine which was communicated to the Royal Medical and Chirurgical Society in Dec. 1867, and published in the 51st vol. of the *Transactions*.* One of the main objects of that paper was to explain the hypertrophy of the left ventricle of the heart, which, as Dr. Bright first indicated many years ago,† is almost invariably associated with the contracted granular kidney, when there is no disease of the cardiac valves or the large arteries to account for the hypertrophy. Dr. Bright sug-

* I. On certain points in the anatomy and pathology of Bright's Disease of the kidney ; II. On the influence of the minute blood-vessels upon the circulation.

† *Guy's Hospital Reports*, vol. i.

gested two alternative explanations. "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 of the heart necessary to force the blood through the distant subdivisions of the vascular system."

In my endeavour to explain the cardiac hypertrophy it occurred to me that the impediment to the systemic circulation which calls for more forcible contraction, with resulting hypertrophy of the left ventricle, might be due to a persistent general contraction of the systemic arterioles, this contraction being excited by the abnormal quality of the blood, just as the arterioles are excited to contract, and so to cause high arterial tension, by the passage of unoxygenised blood into the systemic arteries. Then it seemed reasonable to infer that the long-continued over-action of the arterioles would result in hypertrophy of their muscular walls; and guided by this line of reasoning, I was led, with the aid of my friend and colleague Dr. Kelly, to the discovery that the walls of the arterioles are hypertrophied not only in the kidneys, where I first discovered and described it seventeen years before, but also in the skin, the intestines, the voluntary muscles, and the pia mater. The paper in which these results are described is illustrated by drawings, showing hypertrophied arterioles in each of these tissues.

My friend Dr. Halliburton has lately, at my

request, supplied me with numerous sections from two cases of contracted kidneys, with hypertrophy of the left ventricle, in which the walls of the arterioles are seen to be hypertrophied, not only in the tissues before mentioned, but also in the muscular walls of the heart, in the spleen, and the pancreas. The materials for these sections were supplied from the hospital by my friend, Dr. Dalton, and the sections were made under the supervision of Dr. Halliburton by his two assistants, Mr. Colls and Mr. Lyle. It will be seen, then, that with the hypertrophied left ventricle, in cases of contracted granular kidney, there is associated hypertrophy of the walls of the arterioles throughout the system. On the other hand, the walls of the *pulmonary* arterioles in these two cases are not hypertrophied. The absence of hypertrophy of the pulmonary arterioles is probably the rule in cases of granular kidney.

The persistent contraction, with resulting hypertrophy of the renal arterioles, would appear to be the result of a physiological principle, that when, from structural change or functional incapacity of an organ, the changes which ought to take place in its capillaries do not take place, and the blood consequently is not in a fit state to pass through and from them, the minute arteries, through vaso-motor nerve influence, are thrown into a state of contraction; their stop-cock function is brought into play. This contraction of the renal arterioles is analogous to the contraction of the minute pulmonary arteries, which arrests the cir-

culation through the lungs in the final stage of apnœa (asphyxia); while contraction of the systemic arterioles throughout the body is the result of an abnormal condition of the blood; uræmia in cases of renal disease, deoxidation as a result of apnœa.

That the high systemic arterial tension in the first stage of apnœa has for its proximate cause a deficiency of oxygen and not an excess of carbonic acid is proved by the fact that precisely the same phenomena occur when either nitrous oxide gas or pure nitrogen is breathed, as a result of which there would be a deficiency rather than an excess of carbonic acid in the blood.*

The absence of hypertrophy of the pulmonary arterioles in cases of granular kidney indicates that uræmia does not excite contraction of these vessels, and is consistent with the fact that, as a rule, the cardiac hypertrophy is seen on the left side only. The occasional association of some hypertrophy of the right ventricle may be due to backward pressure from the left side, or to such an impediment in the lungs as results from emphysema.

In the "Pathological Anatomy" of Dr. Wilks and Dr. Moxon, the authors say: "In Bright's Disease, so far as we have observed, hypertrophy is limited to the left ventricle or nearly so limited. The right appears to share a little in the enlargement, but this is probably due to the fact that many of the fibres

* See the author's paper On the Physiology of Asphyxia, and on the Anæsthetic Action of Pure Nitrogen, *Proc. Roy. Soc.* vol. xlix. p. 144; also A Post-graduate Lecture on the Influence of the Arterioles in Relation to various Pathological Conditions, *Brit. Med. Journal*, April 1894.

extend across both ventricles, and no doubt must undergo hypertrophy in their whole length, so as to thicken both ventricles."

Since the walls of all the *systemic* arterioles are found to be hypertrophied in cases of cirrhotic kidney, with hypertrophy of the left ventricle, we may be sure that in a section of the lung the *bronchial* arterioles, if visible, would be found to have hypertrophied walls, though I have not been able to verify this by actual observation. The bronchial arterioles are not easily found in a section of the lung.

I now proceed to describe more particularly the appearance of the hypertrophied arterioles in the granular kidney and in other organs and tissues.

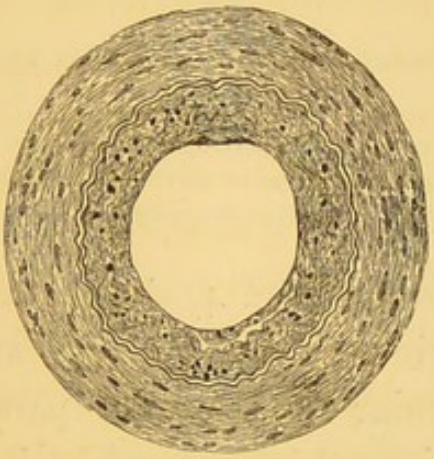

FIG. 3.—TRANSVERSE SECTION OF AN ARTERY FROM A GRANULAR KIDNEY.

The muscular coat much hypertrophied and consisting of several layers of circular fibres. Between the external wavy elastic layer of the intima and the endothelial layer an overgrowth of normal connective tissue. The tunica adventitia, which was inconspicuous, is not represented.—× 200.

Fig. 3 represents the transverse section of a typical hypertrophied renal arteriole. The muscular coat is

seen to consist of several layers of circularly arranged muscular fibres. The inner coat (the intima) consists of three distinct layers, an outer wavy elastic layer in contact with the muscular coat, an inner endothelial layer, and an intermediate layer of connective tissue. The thickening of the intima is entirely due to an overgrowth of the connective tissue between the elastic and the endothelial layer. A longitudinal

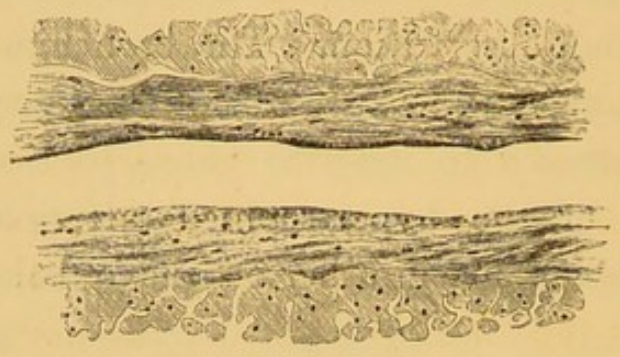

FIG. 4.—LONGITUDINAL SECTION OF AN ARTERY FROM A GRANULAR KIDNEY.

The circular fibres of the hypertrophied muscular coat are seen in section. The longitudinal fibres of the connective tissue of the intima much hypertrophied. The adventitia not shown.—× 200.

section of an artery (Fig. 4) shows that the fibres of the connective tissue take a course at a right angle with the muscular fibres, and parallel with the arterial canal. The chief facts which indicate that this thickening of the intima is the result of a genuine physiological hypertrophy, an overgrowth of a normal connective tissue, are the following. It is always associated with hypertrophy of the muscular coat and while sometimes, though rarely, it equals, it never exceeds the latter in thickness. However great the

thickening of the walls, the canal of the artery retains its uniform cylindrical shape throughout its entire course, so far as can be seen in the field of the microscope.

Now, it would appear that the effect of this thickening of the intima will be to counteract the tendency to elongation of the arterioles by the distending force of the heart, while the hypertrophy of the muscular layer, with its corresponding increase of contractile power, tends to prevent dilatation of the arterial canals. That this is the physiological tendency of the two forms of hypertrophy can scarcely be doubted, but that it is not entirely effectual is proved by the fact that most of the hypertrophied renal arterioles deviate from the straight course of the normal vessels and become more or less tortuous from elongation, while their canals are somewhat dilated. The tortuosity of the artery is shown in Fig. 2, p. 2. In Fig. 4, the artery, so far as it is shown in the drawing, is but slightly curved, but in the specimen from which the illustration is taken, the artery, both to the right and left of the part shown, has taken a sudden bend and is therefore seen in transverse sections. The dilatation of the arterial canals is shown by comparing the well known diameter of normal afferent Malpighian arteries with the arteries in a granular kidney. It scarcely need be said that during life, when the muscular wall is in a state of active contraction, the lumen of the arteries, whether normal or with hyper-

trophied walls, is narrower than it appears in a microscopic section.

On comparing the thickened renal arterioles with those in other tissues, this remarkable difference is apparent—namely, that while the hypertrophy of the *muscular* coat occurs alike in all the tissues, the thickening of the *intima*, so far as I know, is found only in those of the kidneys; but then, on the other hand, the hypertrophied arterioles in other tissues have their external *tunica adventitia* hypertrophied to about the same extent as the overgrowth of the intima in the renal arterioles.

I have specimens from nearly every organ and tissue in which the conjoint hypertrophy of the muscular and the outer coat is apparent. Fig. 1 in Plate I. represents an arteriole from the wall of the heart in a case of granular kidney.

It will be seen that the connective tissue, the fibres of which run parallel with the canal of the artery, is *outside* the muscular coat, and that this, in the hypertrophied artery, is the exact counterpart of the hypertrophied connective tissue *within* the muscular coat of the renal arterioles.

The explanation of this remarkable difference appears to be that the renal arteries, being imbedded in the firm tissue of the kidney, do not, in the normal state, need the support of the tunica adventitia which surrounds the arteries of the pia mater, and those of most, if not all, other tissues; and when, during the progress of granular degeneration of the kidney, the renal arterioles

require to be braced and strengthened in the longitudinal direction, to counteract the excessive force of the hypertrophied left ventricle, this is accomplished by the overgrowth of the connective tissue of the intima.

Some renal arteries, however, show hypertrophy of both the external coat and of the intima. In these specimens the intima is usually less thickened than when the adventitia is inconspicuous. The structure of both these tissues is apparently identical; they are stained alike by logwood, and the cause and physiological purpose of their hypertrophy are probably the same.

I have sections of the vagina, uterus, and bladder of an ape, for which I am indebted to Dr. Heneage Gibbes. Fig. 2, Plate I. represents the transverse section of an arteriole from an ape's vagina. It will be seen that the thick muscular coat and the thick intima present the same appearance as the hypertrophied renal arteriole (see Fig. 3, p. 7).* It will scarcely be supposed that the thick intima of these normal arterioles is the result of any pathological change.

I learnt from Dr. Gibbes that he finds these thick-walled arterioles in organs that are liable to alternations of expansion and contraction, such as the bladder, uterus, and vagina, and they are well seen in the

* The only difference between the renal arterioles and those from the vagina of the ape is that in the latter the elastic layer next to the muscular is not seen, but in many hypertrophied renal arterioles the elastic layer is not visible.

section of each of these organs which I possess. It is remarkable that in none of these thick-walled arterioles is the tunica adventitia apparent; it seems to be replaced, as in most of the hypertrophied renal arterioles, by the thickened intima.

In most sections of a granular kidney there may be seen arterioles, whose walls having been hypertrophied, have subsequently become involved in the atrophic process which affects the glandular tissues of the organ. The atrophy of the walls of the arterioles may be seen in various successive stages. In the early stage the arteriole retains its usual size and form, but the muscular and connective tissues have lost the clear and distinctive features which are represented in Fig. 3, p. 7. As the atrophy proceeds, the arterioles dwindle in size, the distinction between the different layers of tissue is lost, and the walls assume a fibroid appearance (see Plate I. Figs. 3, 4, and 5). These atrophied arterioles are seen in the midst of disorganised glandular tissues, in the degenerative changes of which they have become implicated; and, without doubt, the final result is that many arterioles entirely disappear.

The small object represented in Fig. 5, Plate I., would hardly be recognised as an atrophied arteriole if the successive stages of the wasting process were not readily traced in numerous specimens.

Then it is to be observed that as the granular kidney is the only organ that, as a rule, becomes atrophied during the progress of chronic Bright's Disease, so in no other organ or tissue has it been found that arterioles

whose walls have been thickened by physiological hypertrophy have subsequently become atrophied. It is now quite intelligible that in a section of a granular kidney there may be seen some arterioles with well-nourished hypertrophied walls, while others, after having undergone hypertrophy, are found in various stages of atrophy down to near the vanishing point.

In a typical case of granular kidney, with the exception of here and there an arteriole which, having been hypertrophied, has subsequently become involved in the atrophy which primarily affects the glandular tissues, all the renal arterioles have their walls more or less equally hypertrophied. In fact, the hypertrophy of the arterial walls, not only in the kidney, but in every part of the systemic circulation, is the necessary result of an intelligible physiological law, which requires that the propelling and the resisting and regulating forces by which the circulation of the blood is effected should be equipoised. If the arterioles of any organ or tissue failed to have their walls strengthened in proportion to the increased driving force of the hypertrophied left ventricle, the capillaries which receive the blood from such arterioles would be liable to over-engorgement and to become ruptured. The maintenance of this balance of forces in cases of granular kidney is effected by hypertrophy of the walls of the arterioles in proportion to the cardiac hypertrophy, and apparently to an equal amount in the arterioles of all the tissues throughout the body, with two remarkable and instructive excep-

tions. The exceptions are, that while the *renal arterioles* are more hypertrophied, those of the *pia mater* are less thickened by overgrowth than the arterioles in other parts of the body. The explanation of the relative excess of hypertrophy of the renal arterioles appears to be that, as we have seen, during the progress of atrophic changes in the granular kidney, many of the arterioles become atrophied and disappear. The result is, that the work of regulating the undiminished blood-supply through the renal artery is thrown upon a smaller number of arterioles. Dr. Dickinson has shown, by accurate measurement (see hereafter, p. 40) that the circumference of the artery supplying a granular kidney is larger than that of the artery of a healthy kidney. The excessive hypertrophy of the renal arterioles is an index of the extra work which has been thrown upon each arteriole, in consequence of their diminished numbers. The number of arterioles in the atrophic stage subsequent to hypertrophy varies in different granular kidneys; and I have observed that the more numerous the wasting arterioles are the greater is the compensatory hypertrophy of those that have not become atrophied. There is then conclusive evidence that while the arterioles thrown out of work by destruction of the glandular tissues are wasting, those which are still active are increasing in the thickness and strength of their walls. The diminished vascularity of a granular kidney explains the results of experiments by Dr. Dickinson. The experiments were

performed by passing water with a fixed temperature and pressure into the renal artery and measuring the amount which escaped by the vein in a given time. It was found that a granular kidney could not, on an average, transmit a quarter as much water as a healthy kidney in the same circumstances.*

As the great hypertrophy of the walls of the renal arterioles is a result of the excessive physiological work imposed upon their decreased numbers, so the relatively less hypertrophy of the arterioles in the pia mater appears to be a result of the minute subdivision of the arteries in that tissue; so that a greater number of arterioles are contained within a given space than are found in most other parts. The more numerous the arterioles in which a larger artery terminates, the less is the effort required by *each arteriole* to maintain the balance of the circulation, and the less, therefore, would be the hypertrophy of the arterioles in cases of granular kidney.

It may be that besides the manifest difference in the amount of thickening of the renal arterioles and those of the pia mater, there are less conspicuous variable degrees of thickening in the arterioles of different tissues, which admit of the same anatomical explanation; but that the general result is the maintenance of an exact balance between the propelling and the resisting forces can, I think, scarcely be doubted by any unprejudiced observer of the facts.

* "The Pathology and Treatment of Albuminuria."

The subject is one of exceptional physiological interest, upon which the results of what may be called a natural process of vivisection during the progress of renal degeneration have shed a new light. The prolonged overaction of the arterioles during the progress of chronic Bright's Disease is as clearly indicated and registered by the hypertrophy of their walls as is the increased systemic arterial pressure during the first stage of apnœa (asphyxia) by Ludwig's kymograph.

Section II. Dr. Lionel Beale's Contention that the Thickening of the Arterioles is not the Result of Hypertrophy.

It was not to be expected that my interpretation of the physiological relationship between hypertrophy of the left ventricle and that of the systemic arterioles in cases of granular kidney, novel as it was, would escape criticism.

The first amongst those who publicly dissented from my account of the cardio-arterial changes in Bright's Disease was my friend and colleague, Dr. Lionel Beale. In his work on "Kidney Diseases, &c.," published in 1869, after expressing his belief that I was the first to direct attention to the thickened condition of the arteries in diseased kidneys, he says that the thickening is not hypertrophy, but "it is unquestionably associated with great change and degeneration

of the normal tissue." He also says, "It is more probable that in the morbid change in question the action of the arterial coats is diminished rather than that it is increased, while it is most difficult to understand how anything like *overaction* can possibly occur."

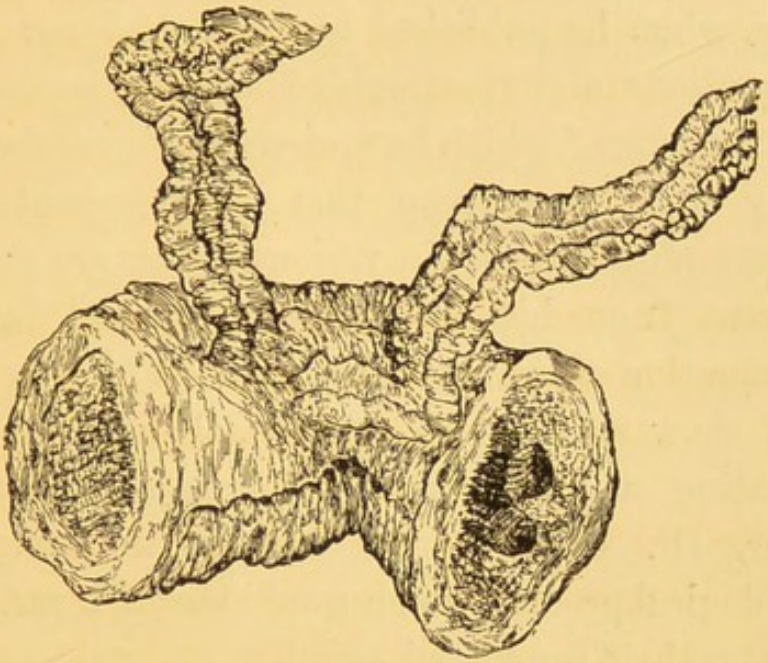

FIG. 5.

The following is Dr. Beale's description of this figure: "Arteries from a fatty and contracting kidney, showing complete degeneration of the muscular fibre cells and the deposition of glistening albuminous material. The walls of the artery have probably long lost all contractile power, and are converted into rigid inelastic tubes, the inner surface of which is uneven, with great irregularity in calibre.—× 215."

On referring to Dr. Beale's illustrations of thickened renal arteries, a portion of one of which is here reproduced, the irrelevancy of his criticism is at once manifest, for his drawings of thickened arteries are obviously

illustrations of *lardaceous degeneration* of the arteriole walls. Arterioles thus degenerated have their contractile power impaired, and, in consequence, they do not resist the onward movement of the blood so as to give rise to hypertrophy of the left ventricle, which is rarely, if ever, found associated with uncomplicated lardaceous disease. Now, although I believe that Dr. Beale, when he published his book, had not seen my preparations of hypertrophied arteries, he must have read the paper * which he undertook to criticise, and he surely must have seen that my representations of hypertrophied arteries in various tissues are essentially different from his drawings of typical lardaceous degeneration of the arteriole walls. While my illustrations show an increase of normal muscular tissue, indicating a corresponding increase of contractile power, Dr. Beale figures arteries thickened by a pathological product which would lessen, if not entirely destroy, their functional activity.

Section III. Sir William Gull's and Dr. Sutton's Hypothesis of "Arterio-Capillary Fibrosis," or "Hyalin-Fibroid Degeneration."

One result of Dr. Beale's unfortunate misunderstanding, and doubtless, therefore, unintentional misrepresentation of my work, was that it appears to have misled the late Sir William Gull and Dr. Sutton,

* *Med. Chir. Trans.*, vol. li.

and thus contributed to the evolution of their remarkable hypothesis of "arterio-capillary fibrosis." In their paper, published in the 55th volume of the *Transactions of the Royal Medical and Chirurgical Society*, these authors make the following statement (pp. 279, 280): "Our observations confirm the opinion that the minute arteries are thickened in chronic Bright's Disease, and we gladly acknowledge the debt the science of Medicine owes to Dr. George Johnson for so distinctly insisting upon the fact. Dr. Beale has also confirmed the accuracy of Dr. Johnson's observations as regards the thickening of the minute renal arteries, and he expressed an opinion that this is due not to hypertrophy of the muscular layer of the vessel, and he has stated that the outer layer of these vessels is thickened."

Again, Sir William Gull, in a clinical lecture on Bright's Disease (*Brit. Med. Journal*, vol. ii. 1872), quotes Dr. Beale's book, and says: "Dr. Beale agrees with ourselves (Gull and Sutton) that the thickening of the vessels has been too hastily assumed to be one of hypertrophy. Dr. Beale's views on this part of the subject—I mean as regards the vascular changes in the kidneys—are entirely in accordance with what has been seen by both Dr. Sutton and myself." Yet, notwithstanding this assertion of identity of views, it is obvious that Dr. Beale's drawings of renal arteries thickened by lardaceous degeneration are as different from Sir William Gull's and Dr. Sutton's representations of their so-called "hyalin-fibroid" change,

as they are from my illustrations of hypertrophied arteriole walls.* The theory of arterio-capillary fibrosis which some writers, influenced perhaps by the deservedly high reputation of its authors, have accepted without question, has been shown by various competent observers to be inconsistent with anatomical facts, with generally accepted physiological principles, and with clinical experience. Amongst other writers Dr. Bryan Charles Waller has very ably criticised the theory in his work on "Interstitial Nephritis."

Sir William Broadbent, in his interesting work on "The Pulse," having shown that the doctrine in question is inconsistent with indisputable facts, expresses his opinion in the following sentence (p. 240): "The hypothesis of a general hyalin-fibroid degeneration, of which the cirrhosis of the kidney is only a part or a consequence, appears to me to have no foundation in fact, and to survive only in virtue of the great and merited reputation of its authors and of the euphonious terms which they introduced." It would seem that a doctrine of which a high authority could speak in such terms, must soon die a natural death, and should now need no serious refutation; but we find that from time to time the hypothesis in question is quoted as if it were indisputably true, and in the second edition of Dr. Sutton's "Lectures on Pathology," edited by Dr. Paul and revised by Dr.

* Compare my illustrations (Figs. 3 and 4, pp. 7, 8) with Dr. Beale's (Fig. 5, p. 17), and Sir Wm. Gull's and Dr. Sutton's (Figs. 8 and 9, pp. 24, 25).

Wilks, the main points of the theory are re-stated by the author, together with his reasons for dissenting from my pathology, so that "he being dead yet speaketh."

In the 58th volume of the *Medico-Chirurgical Transactions* and the 28th volume of the *Pathological Transactions* I have criticised the pathological doctrines of Sir William Gull and Dr. Sutton at some length. Referring to these volumes for a detailed criticism of the hyalin-fibroid doctrine, I will here briefly refer to certain facts and physiological principles which are inconsistent with the hypothesis in question. It is admitted on all sides that the hypertrophy of the left ventricle in cases of cirrhotic kidney is the result of an impediment in the terminal vessels. Gull and Sutton agree with me thus far, but they differ from me in assuming that the immediate cause of the impeded circulation is not persistent contraction of the arterioles, resulting in hypertrophy of their walls, but a form of degeneration, the effect of which would be to destroy or greatly impair the power of the arterioles to regulate the distribution of the blood.

Sir William Gull, in the clinical lecture before referred to, expresses the belief of his colleague and himself, "that hypertrophy of the heart is due to changes in the arterioles and capillaries, whereby their elasticity is diminished, and so the blood retarded." This doctrine implies a belief that the arterioles and capillaries, by their *elasticity,* help to drive the blood onwards, while it ignores the muscu-

larity and the true function of the arterioles. This unphysiological hypothesis is inconsistent with indisputable facts.

Both Sir William Gull and Dr. Sutton, after the reading and discussion of their paper at the Royal Medical and Chirurgical Society, recognised in a microscopic specimen which I showed them, the appearances which they had described and figured as pathological; the specimen in question consisting of normal arterioles from the pia mater of a sheep, the outer coat of which had been distended and rendered hyaline by immersion in glycerine. The authors stated in their paper that all their specimens had been immersed by an assistant in a mixture of glycerine and camphor water before they were examined. The accompanying figures represent the effect of different modes of mounting normal arterioles from the pia mater.

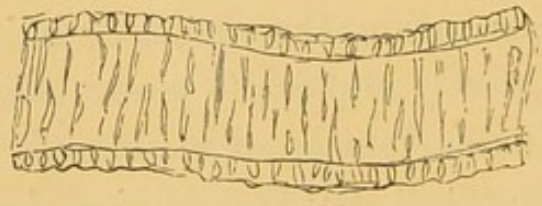

Fig. 6.—Normal Arteriole from the Pia Mater of a Sheep. Mounted in salt and water.—× 200.

Figure 6 shows the appearance of a normal arteriole which has been preserved in salt and water, while Figure 7 indicates the effect of glycerine in distending the tunica adventitia and giving it the hyaline appearance. If the glycerine is made slightly acid

the distension of the adventitia occurs with great rapidity, and if the acidity is afterwards neutralised by ammonia the hyaline distension is removed, so that the artery, having been made to assume the

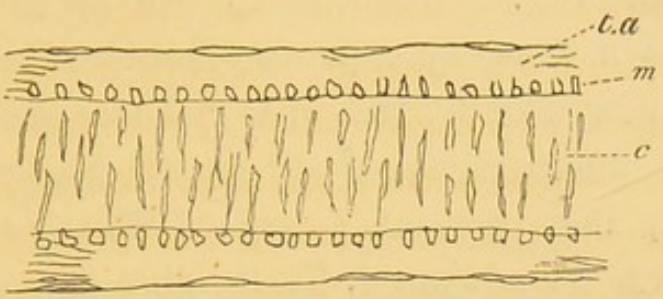

FIG. 7.—NORMAL ARTERIOLE FROM THE PIA MATER OF A SHEEP.

Mounted in glycerine. *t. a*, the Tunica Adventitia. *m*, the Muscular Layer. *c*, Canal of the Vessel.—× 200.

appearance of Figure 7, reverts to the normal condition represented in Figure 6.*

The effect of glycerine, especially when slightly acidulated, is not only to cause hyaline distension of the adventitia, but also to render indistinct the muscular nuclei of the middle coat; and we have a very interesting and instructive proof of this in one of the illustrations appended to the paper of Sir William Gull and Dr. Sutton.† Fig. 7, in Plate VI., represents a transverse section of a highly magnified (× 750) thickened renal artery, which is described as "a minute artery of the kidney, greatly thickened by hyalin-

* The effect of glycerine, especially when slightly acidulated, upon the tunica adventitia, has been well described by Dr. Galabin, "On the Connection of Bright's Disease with Changes in the Vascular System," pp. 13, 14.

† *Med. Chir. Trans.*, vol. lv.

fibroid changes in the outer layer of the vessel," and in their paper (p. 274) the following reference is made to the drawing. "The muscular nuclei were indistinct, and many of them were so altered as hardly to be recognisable. External to the muscular nuclei there was a quantity of hyalin-fibroid substance, and the layer formed by this material was much thicker than the muscular layer" (Plate VI. Fig. 7).

Again, they say (at p. 278) "Where the kidney disease was far advanced, hyalin-fibroid changes were seen in the renal arteries precisely similar to those observed in the vessels of the pia mater and of other parts of the body."

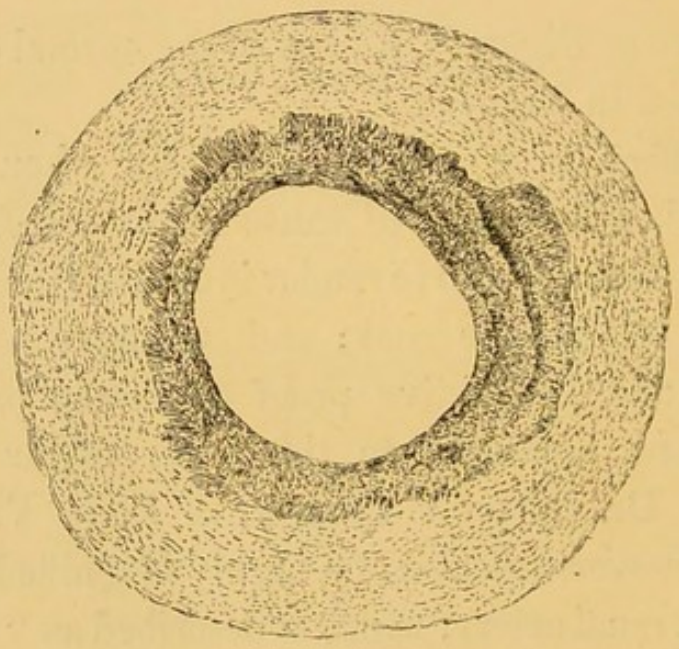

FIG. 8.—TRANSVERSE SECTION OF A RENAL ARTERY WITH THICKENED WALLS.

Reduced by one-third from Fig. 7, Plate VI. of Sir William Gull and Dr. Sutton.—× 500. Reproduced by permission of the President and Council of the Royal Medical and Chirurgical Society.

Fig. 8 is a reduced reproduction of the illustration

referred to, this being the only representation of a thickened renal artery which is given in the authors' paper, and of this specimen they have given a most erroneous interpretation. The inner layer, which they mistake for the muscular coat, is obviously the thickened intima, the fibres of which take a longitudinal course; and as this tissue is not muscular, it is not surprising that "the muscular nuclei were indistinct;" while the outer layer, which the authors suppose to be the counterpart of the "hyalin-fibroid layer in the arteries of the pia mater," is the greatly hypertrophied muscular coat, the circularly arranged nuclei of which have been blurred and rendered indistinct by the action of glycerine.

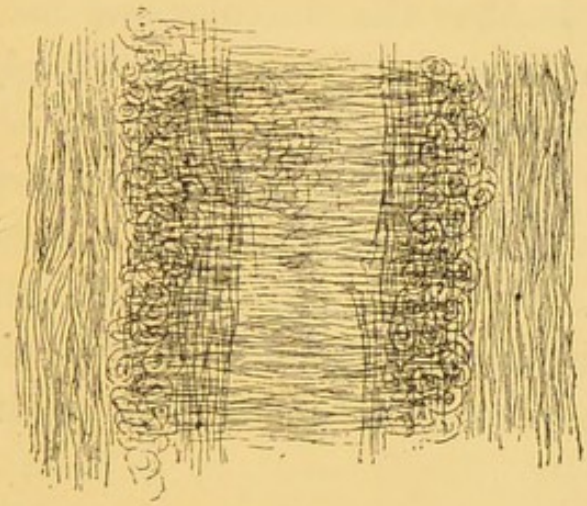

FIG. 9.

Reproduced from Fig. 2, Plate V., of Sir William Gull and Dr. Sutton.
× 750. (See p. 26.)

The tunica adventitia in the renal arterioles is often inconspicuous, and it is not shown in this illustration. It is manifest that this drawing of a renal artery,

which the authors supposed to represent their hyalin-fibroid change, is a conspicuous illustration of muscular hypertrophy.*

Figure 9 is described by the authors as "arteriole [from the pia mater] much thickened by coarse fibroid changes outside the muscular layer; tunica intima thickened also." The effect of the glycerine on this specimen has been to cause swelling of the muscular nuclei, to increase the thickness of the adventitia, and to cause a partial separation of the intima from the muscular coat.† It is very remarkable that the hypertrophied muscular coat, as represented in Fig. 8, should have been supposed to be the counterpart of the thickened adventitia in Fig. 9. The only excuse for the mistake is that the muscular coat had been rendered indistinct by the blurring effect of glycerine.

At a meeting of the Pathological Society in 1877, at which Sir William Gull and Dr. Sutton were present, I pointed out this misinterpretation of their drawing, which they did not attempt to defend. After this exposure of the authors' failure to recognise so conspicuous an example of muscular hypertrophy—the

* Compare Fig. 8 with the transverse section of a thickened renal artery, represented in Fig. 3, p. 7.

† This effect of glycerine has been noticed by Dr. Galabin ("On the Connection of Bright's Disease with Changes in the Vascular System"). He says, with reference to the arterioles of the pia mater, "I have found, as I believe, that in cases of granular kidney both the muscular and external fibroid coats are thickened on the addition of glycerine. The external fibrous coat and the intima become swollen after a time, and the former assumes what has been described as the 'hyalin-fibroid' appearance," p. 13.

case being one in which the "wood was concealed by the trees"—we may disregard such futile objections as that hypertrophy of the muscular wall is difficult to establish, since it is said to be simulated by vessels in a state of contraction, and a fixed standard of thickness of the normal muscular coat cannot be obtained. These objections are based upon imperfect observation. Nothing can be easier than to compare such arterioles as the afferent vessels of the Malpighian bodies, which are remarkably uniform in the diameter of their canals and the thickness of their walls, and it can plainly be seen that the hypertrophied arteries are very much thicker than the corresponding normal vessels (see *ante*, Figs. 1 and 2, p. 2). No amount of *post mortem* contraction of an artery can simulate the appearance of hypertrophy, which consists in an increase of the muscular layers from one to three or four in vessels of equal calibre.

Sir William Broadbent gives some particulars of fatal cases in which there has been an imperfect development of the cardio-arterial changes, as indicated by a pulse of low tension—and I entirely agree with his comment on these cases. He says: "It may be pointed out that cases of fatal disease of the kidney, without thickened arteries and hypertrophied heart [which are cited for the purpose of proving that when such changes are associated with renal disease they are concurrent with, or antecedent to, but not consequent upon it] are simply cases of the kind just exemplified, in which the kidney disease has proved

fatal early, from want of the cardio-vascular changes."

Such cases support the view that the hypertrophy of the left ventricle and of the walls of the arterioles is physiological and conservative.

The hypothesis of arterio-capillary fibrosis is not consistent with the results of experiment or with clinical observation. Sir William Broadbent says ("The Pulse" p. 239): "If the change which gives rise to resistance in the arterioles and capillaries is degeneration or hyalin-fibroid, it must interfere with the contraction and relaxation of which these vessels are normally capable. Relaxation especially should be slow and imperfect. Let then nitrite of amyl be administered to the subject of this supposed fibrosis; if the physiological effects are produced, the muscular fibres of the arterioles and the contractile element in the capillary wall cannot well have undergone structural change or degeneration. This test has been applied, and always with the same result; the full effects of the nitrite are manifested." Sphygmographic tracings from a case of chronic Bright's Disease taken before and after the inhalation of nitrite of amyl are given in confirmation of this statement. This argument was used by Sir William Broadbent when the subject was first discussed at the Royal Medical and Chirurgical Society.

Having already proved that the term "hyalin-fibroid" is significant of a double error, the hyalin appearance being an artificial product of the glycerine

and the thickening of the arterioles not being a result of fibroid degeneration, it remains to be shown that the alternative "euphonious" term "arterio-*capillary* fibrosis" indicates yet another error of observation. Nothing is easier than to demonstrate that, in cases of Bright's Disease, except the Malpighian capillaries, which are always more or less structurally changed by the constant transudation of albumino-fibrinous material through their walls, and which in cases of lardaceous degeneration present the characteristic waxy appearance, the capillaries in the kidney and in every other tissue present no appearance of thickening or structural change of any kind.

FIG. 10.—PORTION OF VEIN AND INTERTUBULAR CAPILLARIES FROM A GRANULAR KIDNEY.

The coats of these vessels present no appearance of thickening; the canals are partly filled by injection.—× 200.

Fig. 10, which is reproduced from the paper in which I first described the hypertrophy of the renal arterioles,* shows that the renal veins and the intertubular capillaries are entirely free from thickening. I have in my possession numerous specimens which show with unmistakable clearness in one part true hypertrophy of the walls of the arterioles, and in other parts the intertubular changes which are charac-

* *Med. Chir. Trans.*, vol. xxxiii.

teristic of advanced renal degeneration ; these altered tubes being in close contact with, and immediately surrounded by, intertubular capillaries in a normal condition. The paper of Sir William Gull and Dr. Sutton in the 55th volume of the *Medico-Chirurgical Transactions* contains two illustrations (Figs. 1 and 2 in Plate VI.) of what the authors believe to be thickened capillaries. The true interpretation of these appearances is doubtful, but amongst the innumerable capillaries that have come under my observation I have seen none like those two figures. It is probable that these straight vessels were small arteries with thickened walls, the structure of which had been rendered indistinct by glycerine.

Although, in the interest of what I believe to be the truth, I have felt called upon to comment on the incorrect observation and the unphysiological reasoning of Sir William Gull and Dr. Sutton, I believe that the publication of their papers has been of real service, by directing more general attention to the important subject of the arterial changes in Bright's Disease.

My belief is that Sir William Gull was misled by Dr. Sutton, to whom, as he said during the discussion of their conjoint paper, " the whole credit of the work was due." Dr. Sutton who, so far as I am aware, had not before published any results of microscopic work, quite honestly misinterpreted the appearance of specimens which had been prepared by an assistant. The joint authors assert that the vascular changes which they describe are " allied with the conditions

of old age," but they admit that "children are occasionally the subjects of granular contracted kidney," and they refer to a typical case in a girl aged nine; but it is remarkable that they make no reference to the appearances—very different from the "hyalin-fibroid" change—which result from senile degeneration of the small cerebral blood-vessels described and illustrated by Sir James Paget* and others.

I have much pleasure in stating that Dr. Sutton did an admirable piece of work, for which he deserves the gratitude of the profession; I allude to his "Report on the Morbid Anatomy of Cholera," published in the 4th vol. of the *London Hospital Clinical Lectures and Reports*. His report fully confirms the accuracy of the statement which was first published by Dr. Edmund Parkes, that after death in the collapse stage of cholera, the right side of the heart is greatly distended, while the left is empty or contains very little blood. This *post mortem* evidence of a greatly impeded circulation through the lungs in the stage of collapse is identical with that which is found after death from acute apnœa (asphyxia).

Section IV. The Hypothesis that the Primary Seat of Obstruction is in the Capillaries.

Some pathologists, while entirely agreeing with me that the thickening of the arterial walls in cases of

* "Surgical Pathology," third edit. p. 106.

granular kidney is the result of true hypertrophy—an overgrowth of normal tissue without structural change—are not in complete accord as to the interpretation of the hypertrophy.

The points of agreement and of difference between Sir William Broadbent and myself are stated in the following sentence (*op. cit.*, p. 237): "Nothing could be more clear than the demonstration of the increase of the muscular fibre-cells in the thickened arterioles of chronic Bright's Disease; and except that, in my opinion, the obstruction is primarily in the capillaries, and the arteriole contraction secondary to this, Dr. Johnson's theory commands my entire adhesion." In more than one part of his work Sir William Broadbent asserts that "resistance in the capillaries is the most frequent and important of the causes of arterial tension" (p. 154). This resistance, he says, "can scarcely be other than some substance present in the blood which acts directly upon the capillary walls, either provoking contraction or affecting the cohesion of the blood and the capillary membrane." Now, while the influence of the arterioles has been proved by the most conclusive experiments, I am not aware of any facts, either physiological or pathological, which lend support to the suggestion that the capillary walls have such a power of contraction, or that, apart from inflammation, which is not here in question, there is such cohesion between the blood and the capillaries as suffices to cause, or even materially to contribute to, the arterial tension, which is fully accounted for by the action of the arterioles, the per-

sistent, excessive contraction of which, in cases of chronic Bright's Disease, has registered itself in hypertrophy of their walls. The theory of capillary resistance was plausible enough in the days of Dr. Alison and Dr. John Reid, but since the discovery of the structure and function of the arterioles and the vaso-motor nervous system, the hypothesis in question, unsupported as it is by facts, is quite superfluous. With all due respect to the few eminent physicians* who have accepted the hypothesis, I venture to compare it with the doctrine of the ancient physiologists, who maintained that the blood passed from the right to the left side of the heart, not entirely through the obviously open channels of the pulmonary artery and veins, but in part, at least, through invisible pores in the *septum ventriculorum*. This curious fancy was not entirely disposed of until Harvey demonstrated that after ligaturing the pulmonary artery, none of the water which had been forcibly injected into the right side of the heart found its way into the left cavities. What would be thought of a suggestion that the rise of water in the pipe of a suction-pump is due *primarily* to nature's abhorrence of a vacuum, and that atmospheric pressure is *secondary to this?*

Sir William Broadbent has shown that the effect of nitrite of amyl in diminishing the blood pressure of chronic Bright's Disease, proves that the walls of the

* An eminent professor of physiology recently wrote to me, "It seems to me very remarkable that even now there should be physicians who refuse to accept the views of physiologists on the importance of the arterioles."

arterioles have not undergone structural degeneration, but it also proves that contraction of the arterioles is the sole cause of the high arterial tension, since there is no evidence that the drug has any other influence on the capillaries than to cause their over-distension by relaxing the arterioles, and so allowing an increased afflux of blood. The flushing of the face which results from inhaling the vapour of amyl nitrite is the exact counterpart of the heightened colour and temperature of a rabbit's ear, which M. Claude Bernard found to result from dividing the vaso-motor nerves of the ear. The arterioles having been paralysed, whether by the drug or by section of vaso-motor nerves, the capillaries become excessively distended and dilated.

The condition of the heart and lungs after death from acute apnœa (asphyxia) affords conclusive evidence of arrested circulation by contraction of the pulmonary arterioles. The right side of the heart, the trunk and large branches of the pulmonary artery are distended with blood, while the pulmonary capillaries and veins and the left cavities of the heart are empty or nearly so. The mass of blood has been arrested just before reaching the capillaries, and extreme contraction of the arterioles gives the only possible explanation of the arrest. Precisely the same condition of the heart and lungs is found after death in the collapse stage of cholera, and this admits of the same physiological explanation.*

* See the author's "Essay on Asphyxia (Apnœa)," and the chapter on "Cholera," in his "Medical Lectures and Essays."

Sir William Broadbent refers to the appearance of capillary hæmorrhages in various parts of the brain, after death from uræmic convulsions, as affording evidence of capillary obstruction, and he says: "If the capillaries were protected by contraction of the arterioles such rupture could scarcely occur" (p. 134). I have often witnessed such capillary hæmorrhages beneath the conjunctiva, and less frequently beneath the skin, after a violent epileptic convulsion, but it appears to me that the true explanation of these capillary hæmorrhages is that they are a result of *backward engorgement of the capillaries through the veins*, consequent on the impeded respiration during the convulsion,* the engorgement being much increased by the pressure of the convulsed muscles upon the veins.

In the chapter referred to in the foot-note, I have shown that the hæmoptysis which often accompanies a fit of asthma has for its immediate cause rupture, not of the *pulmonary* but of the *systemic bronchial* capillaries, the result of backward venous engorgement during the asthmatic paroxysm. The hæmoptysis of asthma and the capillary hæmorrhages, which are often associated with violent convulsions, are, I believe, the result of strictly analogous conditions of the circulation; the rupture of the capillaries being a consequence of intra-capillary pressure, not by the onward course of the blood through the arteries, but by a retrograde

* See the author's "Medical Lectures and Essays," chap. iv. p. 46, On some Results of a Retrograde Engorgement of the Blood-vessels.

engorgement through the veins. The late Dr. Hyde Salter, an excellent clinical observer and an accomplished physiologist—in the first edition of his work on "Asthma," attributed the hæmoptysis which often attends an asthmatic paroxysm to rupture of the *pulmonary* capillaries, but in the second edition (pp. 88 and 160), he adopts the explanation which I have here given, and attributes the blood-spitting to a retrograde engorgement of the *bronchial* veins and capillaries. After explaining my theory he says: "I believe he is perfectly right; I believe he has solved the difficulty, and his solution satisfactorily explains to my mind, not only the source of apnœal hæmoptysis but what I never could well understand before, the invariable sequence of bronchial mucous exudation upon any form of protracted partial apnœa; for that which would produce bronchial hyperæmia, even though passive, would necessarily produce an increase of the bronchial secretion."

Another example of ruptured capillaries by backward engorgement through the veins is afforded by the petechiæ beneath the pleura and pericardium which are usually seen after death from acute apnœa (asphyxia). In the last stage of apnœa, while the systemic arteries are nearly empty, the veins are extremely distended. Each of the forms of capillary hæmorrhage here referred to is an indirect result of contraction of the pulmonary arterioles, which, while it impedes the onward movement of blood into the systemic arteries, causes a corresponding accumulation

in the veins, with passive engorgement and rupture of the capillaries.

The main function of the arterioles in the normal state is to ensure a constant uniform pressure within the capillaries, this equable pressure being favourable for the free interchange of materials between the blood and the various tissues which is constantly occurring through the thin capillary walls.

Professor Huxley describes the differing functions of the arterioles and the capillaries in the following sentences: "While the small arteries lose the function which the capillaries possess of directly irrigating the tissues by transudation, they gain that of regulating the supply of fluid to the irrigators or the capillaries themselves. The contraction or dilatation of the arteries which supply a set of capillaries comes to the same result as lowering or raising the sluice-gates of a system of irrigation canals" ("Lessons in Elementary Physiology").

Professor Huxley's comparison with the action of "sluice-gates" and mine with that of "stop-cocks," indicate an identity of view as to the regulating function of the arterioles, this view of their action being that of all modern physiologists.

Dr. Dickinson, who inclines to the opinion that the impeded circulation in cases of renal disease is in part at least due to capillary obstruction, says that the capillaries "have been proved to be contractile though they are not muscular" (*Lancet*, July 20, 1895). The authority for this statement is a paper by

Dr. Roy and Dr. Graham Brown (*Journal of Physiology*, 1879, p. 80). I have carefully read that paper, and I find that while the authors conclude that "the capillaries contract or expand in accordance with the requirements of the tissues through which they pass," they neither suggest nor do they mention any facts which indicate that these thin-walled vessels offer any material impediment to the onward passage of the blood, such as would cause hypertrophy of the arterioles, distension and thickening of the large arteries, and hypertrophy of the left ventricle.

Some writers appear to assume that the degree of arterial tension is an index of the amount of intra-capillary pressure, but, so far is this from being true as a general statement, the reverse condition is sometimes found to exist. If in cases of renal disease the increased driving force of the heart is not counterbalanced by an equivalent power of contraction in the arterioles, a pulse of low tension may be associated with excessive pressure in the capillaries and, as a consequence with an increase of albuminuria and dropsy.

And, on the other hand, in cases associated with high arterial tension, the resistance offered by the contracting arterioles may be, and usually is, sufficient to prevent an excess of intra-capillary pressure.

All clinical observers are agreed that in most cases of acute renal disease there is a temporary increase of arterial tension and of the cardiac impulse; the

explanation being that the arterioles are excited to contract by the abnormal condition of the blood. When the disease takes a favourable course the blood is purified by a free secretion of urine, and the high arterial tension gradually subsides. When, on the other hand, the renal disease passes into a chronic stage, the arterial tension continues and increases, and the heaving cardiac impulse, with reduplication of the first sound, indicates the progress of hypertrophy of the left ventricle.

Even in the advanced stages of chronic renal disease the arterial tension may be temporarily lowered by agents which relax the arterioles—not only by nitrite of amyl, as already mentioned, but also by nitro-glycerine and other drugs, which are sometimes used with doubtful advantage, as therapeutic agents. There is an obvious danger in the sudden great relaxation of the arterioles, by which a powerful heart is permitted to exert its full force upon the unprotected capillaries, with the not improbable result of their over-distension and rupture. I once inhaled for a few seconds the vapour of amyl nitrite, an experiment which I should not care to repeat, for, together with the flushing of the face, every beat of the heart was felt as a painful throb within the brain. The regulating function of the arterial stop-cocks was for a time suspended, with extremely disagreeable results.

Section V. Changes in the Large Arteries.

One constant result of the long-continued resistance by the arterioles is that the larger arteries, being forcibly distended by the hypertrophied left ventricle, become thickened, dilated, and tortuous. This may be easily observed in the radial and temporal arteries. The tense, hard, radial pulse, the artery standing out like a cord, which can be rolled under the finger, is an important sign of granular kidney in an advanced stage.

Dr. Dickinson has carefully measured the thickness of the walls and the circumference of numerous arteries from the subjects of granular kidney, and compared them with the corresponding normal arteries. The amount of thickening, though constant, is but small as compared with the much greater proportionate thickening of the arterioles. For instance, the thickness of the normal renal artery as compared with that of a granular kidney is in the proportion of eighteen to twenty-five (*Lancet*, July 20, 1895).

Now, the arterioles in a granular kidney may often be seen to be three or four times thicker than the corresponding normal vessels. The arterioles have become hypertrophied by the long-continued over-action of these vital stop-cocks, while the thickening of the larger arteries is a result, partly of the *passive* resistance offered to the strain caused by the hypertrophied left ventricle behind and the resisting arterioles in front, partly of the *active contraction* of the muscular elements

in the arterial walls, the effect of which is to assist in driving the blood onwards. The thickening of the arterial walls is mainly due to an increase in the number of alternate layers of muscular and elastic tissue, of which the middle coat of the large arteries is composed (See Plate I. Fig. 6). This middle coat of the large arteries is commonly described as the *elastic* layer, the vital contraction of the muscular elements being ignored.*

During life the propulsion of the blood is assisted by the conjoint action of the elastic and the muscular tissues in the arterial walls, but the complete emptying of the arteries after death—which led the ancient anatomists to describe the arteries as air-tubes†—must be due to the closure of their canals by muscular contraction. The mere physical resiliency of the elastic tissue could do no more than reduce the canal of an artery to the diameter which it had before being distended and dilated by the ventricular systole.

Dr. Dickinson has the merit of having been the first to make exact measurement of the amount of thickening and dilatation of the larger arteries, but the general fact has been a matter of clinical observation for a number of years. Thus Sir Wm. Broadbent says, "The

* Dr. Dickinson, on the contrary, in the lecture above referred to, speaks of the middle coat of the large arteries as *muscular*. The anatomical difference between the larger propelling arteries and the regulating arterioles is that while the middle coat of the former contains a combination of muscular and elastic tissues that of the latter is entirely muscular.

† The most plausible etymology of artery is ἀήρ, air or spirit; τηρέω, to keep or preserve. See the article, Arteries, in the New Sydenham Society's "Lexicon of Medicine and the Allied Sciences."

hard pulse and thickened arteries had been early noted when Dr. George Johnson advanced his well-known theory to explain the facts" ("The Pulse," p. 236); and so long ago as the year 1850, during the discussion of the paper in which I first described the thickening of the renal arterioles, Mr. (now Sir James) Paget inquired "whether the author had directed his attention to the smaller branches of the arteries in the body generally as well as those of the kidney, and whether he had found them also hypertrophied. He (Mr. Paget) said he had often observed that in cases of hypertrophy of the left ventricle of the heart without disease of the valves, a state so often met with in chronic disease of the kidney, the larger arteries were increased in size" (*Lancet* Report of the discussion, vol. i. 1850, p. 309). It was not until seventeen years afterwards that I was able to give an affirmative answer to Sir James Paget's sagacious and suggestive question.*

One occasional result of the continued strain to which the larger arteries are subjected is the occurrence of inflammatory and degenerative changes in the arterial tissues; a concurring cause of these changes being probably the morbid condition of the blood. I am indebted to my friend, Professor Halliburton for sections of a cerebral artery about an eighth of an inch in diameter from a case of contracted granular kidney, with a history of inveterate gout. In some sections of this artery the tissues

* See my paper in the fifty-first volume of the *Transactions of the Royal Medical and Chirurgical Society.*

present a normal appearance, while in others, from a different part of the same artery, there is a one-sided thickening of the vessel encroaching on the lumen, and in these parts all the normal textures have been replaced by fibroid tissue, probably a result of gouty degeneration. (See Plate II. Fig. 7).

This specimen affords a good illustration of the contrast between true physiological hypertrophy of the arterial walls and pathological changes in an artery. While the former affects in an equal degree the walls of *all* the arteries in an organ, leaving their canals open, degenerative changes occur in only *some* of the arteries, leaving others free, and, as in this case, the changes may be limited to parts of the same artery, while the canal of the vessel is encroached upon and distorted.

One of the most disastrous results of the strain to which the arteries are subjected between the strongly acting left ventricle and the resisting arterioles is the rupture of a cerebral artery; in consequence of which blood is driven from the torn vessel into the substance of the brain. In a large proportion of cases of granular kidney sanguineous apoplexy is the immediate cause of death.

Section VI. The Thickening of the Arterioles is not the Result of Inflammation.

There yet remains to be noticed and criticised another explanation of the thickening of the arterioles in the contracted granular kidney, namely, that which attributes the changes to inflammation. The terms *endarteritis* and *arteritis deformans* or *obliterans* have, by the authors of this explanation, been supposed to be appropriate. It is scarcely conceivable that those who thus designate the thickening of the renal arterioles can have carefully compared the hypertrophied arterioles with arteries which have been the seat of unquestionable inflammatory changes. I now proceed to do this, and to indicate the essential points of difference between the two contrasted conditions. Fig. 3, p. 7, represents a transverse section of a typical hypertrophied renal arteriole. The muscular coat is seen to consist of several layers of circularly arranged muscular fibres, while the intima is thickened by an overgrowth of normal connective tissue, the canal of the artery being open and retaining its normal form. Compare this with Fig. 2, Plate I., representing the transverse section of a normal artery from the vagina of an ape. It will be seen that the two illustrations represent identical structures.

Then contrast the description and the illustrations of hypertrophied arterioles which have before been

given with authentic records and illustrations of arteries which have been the subject of an inflammatory process. The 28th volume of the *Pathological Transactions*, contains such a description, with illustrations of syphilitic disease of the cerebral arteries by three eminent physicians, Dr. Greenfield, Dr. Gowers, and Dr. Thomas Barlow.

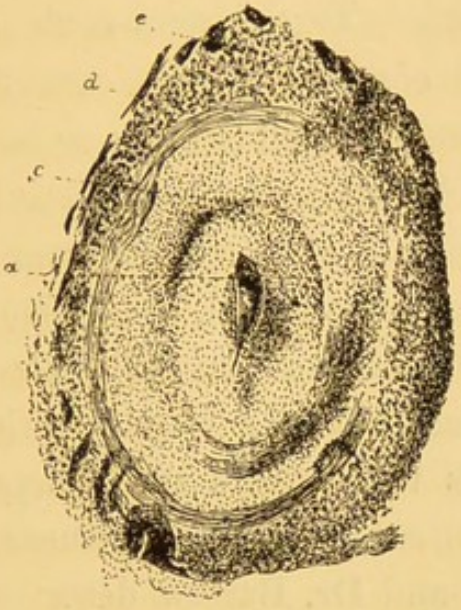

FIG. 11.—SECTION OF SMALL ARTERY OF CEREBELLUM.—× 30.

a. Lumen of vessel; *c*. Thickened inner coat; *d*. Muscularis or middle coat; *e*. Outer coat.

Reproduced from Fig. 2, Plate XIII. *Path. Trans.*, vol. xxviii., by permission of the President and Council of the Pathological Society.

Fig. 11 is a reproduction of one of Dr. Greenfield's illustrations. The difference between this and my illustrations of hypertrophied arteries will be at once apparent. In giving brief extracts from the author's description of the specimen, those parts which indicate the essential difference between an inflamed

artery and one with hypertrophied walls are placed in italics. Dr. Greenfield, describing the above illustration, says, "The coats of the vessel are enormously thickened, and *the lumen of the vessel correspondingly diminished, so as to become a mere narrow chink* (the vessel being cut a little obliquely"). Again, "The muscular coat is of pretty uniform thickness except at some points *where it is invaded by cell infiltration from the outer coat.* The inner coat is enormously thickened and consists of two concentric rings, the boundary between which is more or less defined. . . . . It is to the thickened intima that special attention must again be directed. This will be seen at some points to be enormously thickened, *measuring more than twice as much as the outer and middle coats together.*" We have before seen that in a renal arteriole with hyperprophied walls the intima rarely equals and never exceeds the muscular coat in thickness (p. 8).

Dr. Gowers and Dr. Barlow describe and represent by drawings essentially the same appearances in arteries which have been the seat of syphilitic inflammation.

I have specimens of syphilitic arteritis prepared by Dr. Heneage Gibbes, in which the pathological changes above described are clearly seen; one in particular, in which the enormously thickened intima has pushed the muscular coat outwards and the endothelial layer inwards, a morbid change which was first minutely described by Huebner.

Now, the contrast between the uniform thickening

of the arterial walls which have become hypertrophied and the deforming changes which result from arteritis are sufficiently manifest. The hypertrophy by which *all* the arterioles, not only in the kidney but in every part of the systemic circulation, have been thickened, is a conservative process, by which the functional power of the arterioles is increased, and so the physiological balance between these small vessels and the hypertrophied left ventricle is maintained. On the other hand, the arteries which, here and there, have been the seat of inflammation, while others in the immediate neighbourhood appear quite normal, are thickened and distorted by a process which is purely pathological and destructive, a process which invades not only the walls but the canals of the arteries, and so destroys or greatly impairs their functions.

While the lumen of the arteries which have been the seat of inflammation is distorted, narrowed, and sometimes nearly obliterated, that of the hypertrophied arterioles, as we have seen, retains its uniform diameter; and although, as a result of muscular contraction during life, the canal of these arteries is without doubt more or less uniformly narrowed, in microscopic sections, it appears to be dilated as compared with that of corresponding normal arteries. The explanation of this dilatation has already been given (p. 9).

Dr. Green's "Introduction to Pathology and Morbid Anatomy" contains an excellent illustration of a renal arteriole with hypertrophy of all its coats, and of this the author says—in the 6th edition—the

muscular hypertrophy "is undoubtedly the most prominent structural change." In the 8th edition of the work, which is edited by Dr. H. Montague Murray, the same illustration is given, but the thickening of the intima is assumed to be a result of endarteritis, which "most closely resembles that form which has been described as syphilitic." Yet the contrast between Fig. 188, which shows renal arteries with hypertrophied walls, and Fig. 153B in the same work, showing syphilitic disease of the cerebral arteries, is great and indisputable. In the one, each arterial tunic is thickened by an overgrowth of normal tissue, while the lumen is clear and unencroached upon. In the other, all the coats are infiltrated by a morbid product, the lumen is diminished, and the canal of the vessel is occupied by a clot.

It is remarkable that some writers, while admitting the hypertrophy of the muscular coat of the arterioles of the kidney, attribute the thickening of the intima to endarteritis. This is done by so accurate an observer as Sir William Roberts, as appears from the following extract ("On Urinary and Renal Diseases," 4th edit. p. 442): "The arteries of the kidney show considerable changes; they may show thickening of all their coats. Dr. George Johnson first pointed out the great increase in the muscular coat, and although his position has been attacked by some it has been abundantly confirmed by other observers. . . . . The adventitia frequently shows fibrous thickening, which merges into the connective tissue of the kidney, while

the intima very often is the seat of endarteritis which may considerably diminish the lumen of the vessel."

The concluding portion of this sentence is not quite accurate. We have seen that the lumen of the arterioles in the granular kidney is rather increased than diminished; and while the muscular coat and the intima are both thickened, it is in the highest degree improbable that one is the result of a true physiological overgrowth and the other a product of inflammation, which encroaches neither upon the muscular coat without, nor upon the canal of the artery within.

I believe that Sir William Roberts will be convinced by the facts, arguments, and illustrations which have been set forth in this treatise, that the thickening of the intima in the arterioles of the cirrhotic kidney is *not* the result of endarteritis.

PART II

THE PATHOLOGICAL CHANGES IN THE URINIFEROUS TUBES OF THE CONTRACTED GRANULAR KIDNEY.

THERE exists amongst writers on Pathological Anatomy a more or less general agreement with regard to the structural changes observed in and between the uriniferous tubes of the contracted granular kidney.

In Dr. Dickinson's well-known work on "Albuminuria," Fig. 1, Plate X., is thus described: "A large expanse of finely nucleated tissue is seen passing inwards from the capsule, separating the tubes and surrounding the Malpighian bodies."

In Dr. Green's "Introduction to Pathology and Morbid Anatomy" [8th edit.], Figs. 186 and 187 represent essentially the same appearances with the following description: "*Interstitial Nephritis.* A very advanced stage of the process, showing the large amount of tissue between the tubes of the cortex and the extensive atrophy of the tubes." Again, in

Dr. Bryan Charles Waller's treatise on the "Microscopic Anatomy of Interstitial Nephritis," Plate VII. is thus described: "Cystic kidney. Shrivelled and denuded tubes, and arterioles with hypertrophied media are seen amongst the increased interstitial tissue."

The picture of the microscopic appearances given in these three works and the interpretation of the appearances are practically identical. It is assumed that the primary and essential pathological change is the formation of an intertubular tissue and that the intratubular changes are secondary, the atrophy of the tubes especially being a result of compression by the newly formed interstitial tissue.

The appearances which are figured and described by these and other authors may be seen in almost every section of a granular kidney; but then arises the important question of interpretation. In addition to the structural changes described and figured by those who accept the theory which is implied in the term "interstitial nephritis," there may be found in well prepared specimens, other appearances which are not explained by the doctrine in question and which seem to be inconsistent with it. I will now endeavour to describe and illustrate the chief of these appearances.

The convoluted tubes of the cortex are the chief seat of structural changes. In some sections of the cortex of the kidney there may be found tubes presenting a normal appearance, but these are rare. Many tubes present the appearance represented in Fig. 12. The epithelial lining has become disintegrated and for

the most part removed, appearing in the urine in the form of granular casts. The transverse sections

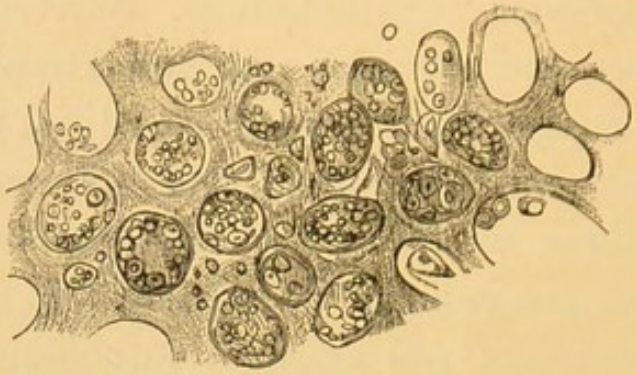

FIG. 12.—TRANSVERSE SECTIONS OF TUBES, CONTAINING ONLY GRANULAR DÉBRIS OF EPITHELIUM.

At one end of the section the contents of the tubes have been washed away, and the sections of the basement-membrane form three empty rings.—× 200.

of tubes in this condition have somewhat the appearance of isolated globular cysts, and they have been so described by more than one observer.

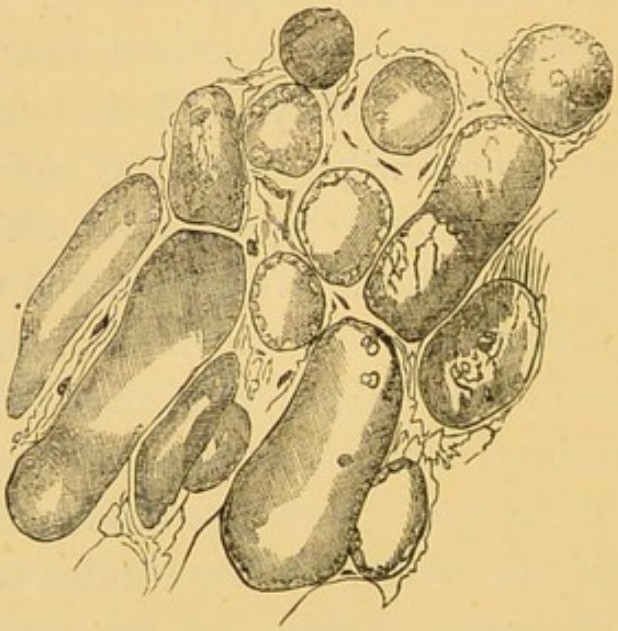

FIG. 13.—TUBES MORE OR LESS COMPLETELY DENUDED OF EPITHELIUM.

Some transversely divided and cyst-like ; others seen lengthwise. × 200.

When, in the same section, some tubes appear transversely divided while others present themselves lengthwise, as in Fig. 13, but all having the same structure and contents, it is easily seen that the cyst-like appearance is given by transverse sections of partially or completely denuded tubes.

Some of the denuded tubes are seen to be filled with a so-called hyaline or colloid material. This material often appears in the urine in the form of "large hyaline casts." Some scattered nuclei appear in the structureless intertubular spaces.

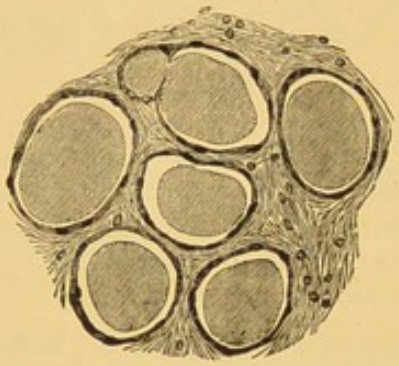

Fig. 14.—Denuded Tubes filled with Hyaline Material.

The shading indicates the stain of the hyaline material by the logwood dye. Scattered nuclei in structureless interspaces.

(Fig. 14).—These are the remains of epithelial nuclei after the tubes which contained them have become atrophied.

In Plate II. Fig. 8 may be seen remarkable changes within tubes in close contact with each other, the only tissue between them being capillaries, the nuclei in whose walls are visible. Most of the tubes contain a hyaline material, the dark shading of which represents the logwood stain as seen in the specimen from which the drawing is taken. In some tubes no epithelium is visible, others contain altered epithelium, and in others again the normal epithelium is replaced by round cells which do not take the logwood stain.

These intratubular changes are unassociated with any form of interstitial deposit, which, if present, would not explain the appearances in question. The replacement of the normal epithelium by round colourless cells is well shown in Fig. 15.

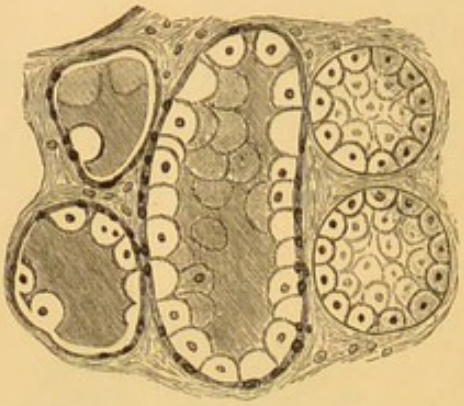

FIG. 15.—SECTIONS OF TUBES IN WHICH A LAYER OF TRANSPARENT CELLS, EACH WITH A SINGLE NUCLEUS, HAS TAKEN THE PLACE OF THE NORMAL EPITHELIUM.

One tube is seen lengthwise. In three of the segments a hyaline material, coloured by the logwood dye, is seen within the cell lining.

This remarkable intratubular change was described and illustrated independently, but with a different interpretation, by Mr. (now Sir John) Simon and myself, in papers which appear in the thirtieth volume of the *Medico-Chirurgical Transactions*, published in 1847.

The destruction of the epithelium results in atrophy of the tubes, as represented in Fig. 16.

The explanation of the wide interspaces between the contracted tubes will presently be given. In some tubes the basement membrane appears to have undergone a hyaline thickening, as if by some change in the epithelial lining, Plate II. Fig. 9.

This, no doubt, is the appearance referred to in the following extract from Handfield Jones' and Sieveking's "Pathological Anatomy" (2nd edit. p. 688). "We have also seen, what we think has not yet been

described, a kind of thickening or hypertrophy of this membrane [*i.e.*, basement membrane of the tubes], which has seemed to us to result from the atrophy of the epithelium and its fusion into an homogeneous layer on the inner surface of the tube."

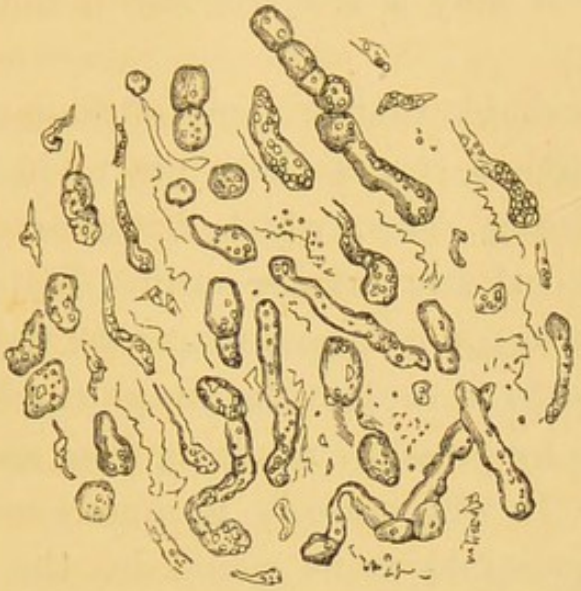

FIG. 16.—TUBES IN PROCESS OF ATROPHY AND CONTRACTION AFTER THE DESTRUCTION OF THEIR EPITHELIAL LINING, A FEW GRANULAR PARTICLES ONLY REMAINING WITHIN THEM.

Wide structureless spaces between the tubes.—× 200.

In transverse sections of these tubes with thickened hyaline walls the epithelial nuclei may be seen irregularly clustered within the lumen. In the next stage of atrophy the walls of contiguous tubules become, as it were, fused together, the appearance of tubular structure is lost, and the nuclei are irregularly scattered over this part of the field of the microscope. This I believe to be the true explanation of the so-called "finely nucleated tissue." The nuclear bodies, which have been assumed to be an interstitial exudation, are,

in fact, the surviving nuclei of the intratubular epithelium. There is a yet further stage of atrophy which can without difficulty be traced; this consists in the disappearance of most of the nuclei, leaving "a large expanse" of a nearly structureless hyaline material with only a few remains of nuclei, Fig 16, p. 55.

It is remarkable that in many of these nearly blank and structureless spaces there are to be seen small blood-containing veins, which in transverse section retain their perfectly circular outline, Plate II. Fig. 9.

This fact again is inconsistent with the hypothesis which attempts to explain the atrophy and contraction of the tubes by pressure resulting from an interstitial exudation. It will scarcely be questioned that the easily compressible veins would be the first to be obliterated by that form of pressure.

Then it is to be observed that while in the cortical portion of a granular kidney some connective tissue may be seen passing inwards from the capsule,* and some also in connection with the external tissue of the arteries, there is no appearance of connective or any form of fibroid tissue in the wide interspaces, the microscopic analysis of which I have here described and illustrated.

One inevitable result of an intertubular deposit would be obliteration of the capillaries, which would

* These offshoots of connective tissue from the capsule occupy the position of the septa between the lobes, which in the fœtus are divided by deep fissures, but which afterwards coalesce. See the author's treatise on "Diseases of the Kidney," 1852, p. 11.

render the gland pallid from anæmia, but the term *red granular kidney* implies that no such condition exists. Another result of an extensive intertubular deposit must be backward engorgement of the Malpighian capillaries and a copious escape of albumen; but it is notorious that in cases of cirrhotic kidney the urine is less albuminous than in any other form of Bright's Disease.

The result of repeated long and careful investigations is the conclusion that the wide expanse of material between the tubes contains the wasted remains of the original tissues, tubular and vascular, apparently blended together by the colloid material which is contained in many of the tubes, and not a new interstitial formation. In other words, these irregular interspaces are the result and not the cause of the atrophy and contraction of the tubes.

The most probable explanation of these structural changes is that some abnormal materials in the blood—the products of over-feeding or of defective digestion, gouty or otherwise; some products of alcoholism, the poison of lead, the retained secretions of other excretory organs, such as the skin and the liver—some of these noxious substances, during the process of excretion by the kidneys have a destructive influence on the renal gland cells. Now, looking at the matter physiologically—and the question is a physiological one—how great is the *a priori* improbability that this excretory process should produce structural changes, not in the gland cells, which are the active agents in the

process, but in the intertubular tissue, that tissue being the capillaries which, wherever visible, are seen to be quite normal.

Many years ago I first published the fact, which I have often observed, that when, in cases of jaundice, bile is largely excreted by the kidneys, the epithelial cells of the convoluted tubes commonly appear in the urine; some of the cells being free, while others are entangled in casts of the tubes. The urine, too, often contains more or less albumen ("Diseases of the Kidney, 1852"), p. 108.

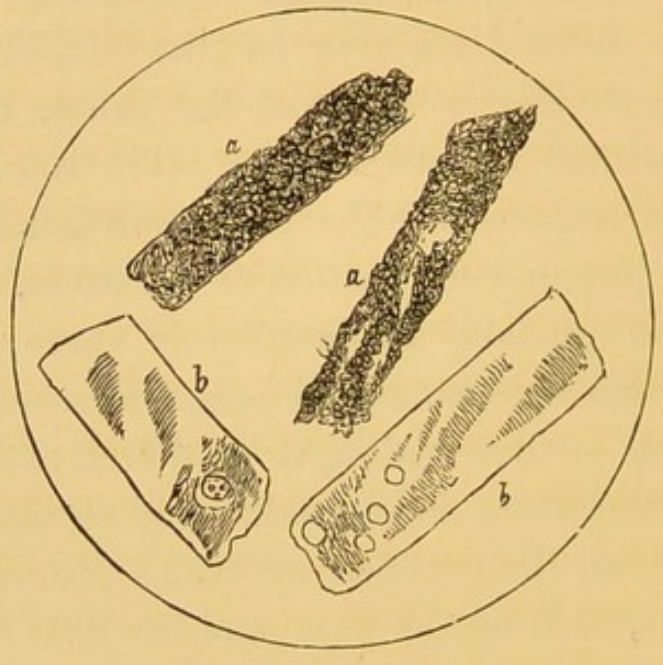

FIG. 17.—*a a*. Granular casts; *b b*. Large hyaline casts from tubes denuded of epithelium.—× 200.

Amongst the earliest signs of the form of chronic degeneration which results in the so-called cirrhotic kidney is the appearance in the urine of granular casts, indicating disintegration of the glandular

epithelium. In the advanced stages of the disease, with the granular casts, are often seen large hyaline casts composed of a material similar to that found in the tubes of the kidney (Fig. 17).

The gland cells are the most delicately organised and most vital structures of the kidney, and their destruction results in atrophy of the uriniferous tubes.

The destruction of the tubular structures involves, as a consequence, secondary changes in the blood-vessels; some arterioles, whose walls have been thickened by a true physiological hypertrophy, subsequently, as we have seen, become more or less atrophied and some Malpighian glomeruli become converted into nearly structureless hyaline masses; without doubt, too, many intertubular capillaries and veins become obliterated. It is now generally agreed that the cysts which are often found in these granular kidneys have their origin in dilatations of tubes, the outlet of which has become obstructed. They belong to the class of so-called "retention cysts."

There appears to be a close relationship between the formation of renal cysts and the appearance of tubes lined by the peculiar round uni-nucleated cells which have been before described and illustrated (See Fig. 15, p. 54).

This, at any rate, is certain, that the contracted granular kidney is the only form of Bright's Disease in which cysts and tubes lined by the peculiar cells in question are constantly found associated. It is probable that these cells continue to secrete a watery

liquid, the escape of which, being prevented by the semi-solid hyaline material which many of the tubes contain, leads to the formation of retention cysts.

Dr. Conway Evans* has recorded a case in which one kidney was of the normal size and appeared outwardly quite healthy, while the other appeared to be honeycombed with cysts. Both kidneys, however, presented the microscopic appearances characteristic of granular kidneys; and, in particular, many tubes were lined by "round or oval transparent cells, each containing in its interior a single well-defined nucleus." This case proves that a great development of cysts may occur with little or no contraction of the gland; since the right healthy looking kidney weighed four ounces and a quarter, while the left, which was in a more advanced stage of cystic degeneration, weighed five ounces.

The Malpighian Bodies undergo various changes. The capillaries often appear thickened and opaque, with an unusual number of nuclei either in or between their walls (see Fig. 18). The capsule is thickened and assumes a fibrous appearance. In some cases the Malpighian capillaries undergo a hyaline or colloid change. In Plate II. Fig. 11, the outline of some of the capillaries is seen, but in extreme cases the glomerulus is converted into a homogeneous colloid mass, all trace of the capillaries being lost. A Malpighian body thus changed may be distinguished

* *Pathological Transactions*, vol. v. p. 133.

from a dilated tube containing colloid material by the appearance of the surrounding thickened Malpighian capsule. Some Malpighian bodies appear atrophied and shrunken, but that in some parts of a section they have not shared in the atrophy of the tubes is shown by the fact that in consequence of the shrinking of the tubes three or four or more of these bodies are sometimes seen in close contact.

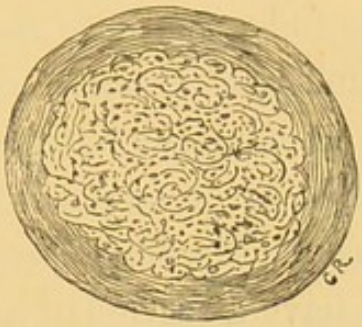

FIG. 18.—MALPIGHIAN BODY—THE CAPSULE THICKENED AND HAVING A FIBROUS APPEARANCE. THE CAPILLARIES THICKENED AND OPAQUE; THE NUCLEI VISIBLE IN THEIR WALLS.—× 200.

Dr. Dickinson, in his "Pathology and Treatment of Albuminuria," gives a good illustration of numerous Malpighian bodies aggregated in consequence of destruction of the tubes. Now, if the destruction of the tubes is, as Dr. Dickinson asserts, "consequent upon the contraction of fibrous tissue," I venture to ask how it happens that these numerous Malpighian bodies have escaped the destructive compression, and have retained their globular form? If, as I have endeavoured to prove, atrophy of the tubes is a result of destruction of their gland-cells, it is quite intelligible that the associated Malpighian bodies, whose office it is to secrete the liquid but not the solid constituents of the urine, should be less liable to the atrophic process.

If the account which I have given of the structural changes in the so-called cirrhotic kidney is as correct as I believe it to be, it is obvious that the term *interstitial nephritis* must tend to stereotype and perpetuate an erroneous doctrine. Since the pathological process is neither primarily interstitial nor is it of the nature of inflammation, it would be more correct to designate the cirrhotic kidney the *atrophic granular kidney*.

I have a section of a kidney which has been affected by acute interstitial nephritis following stricture of the urethra. Throughout the specimen there is a large interstitial accumulation of leucocytes; while in some parts the epithelium in tubes which are surrounded by the interstitial accumulation is seen to be quite normal. In this case, therefore, the etiology was as different from that of the granular kidney as are the microscopic appearances.

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Plate I.

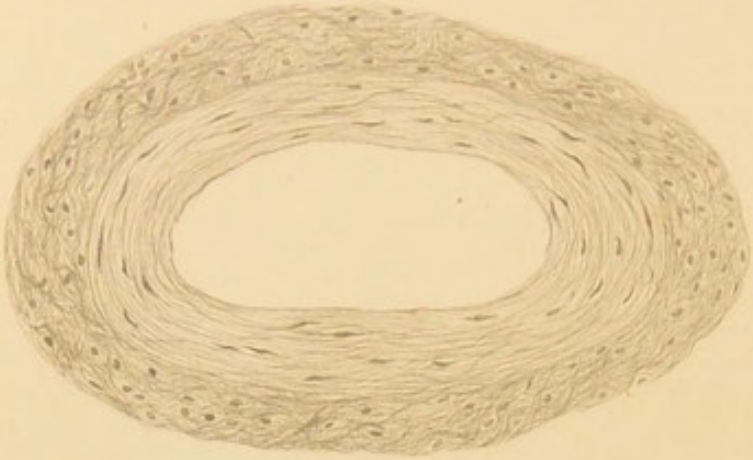

Fig. 1.

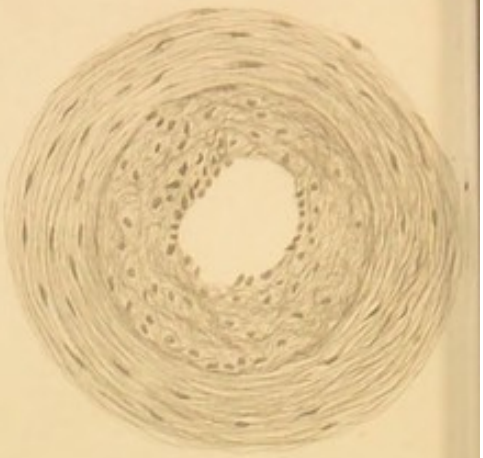

Fig. 2.

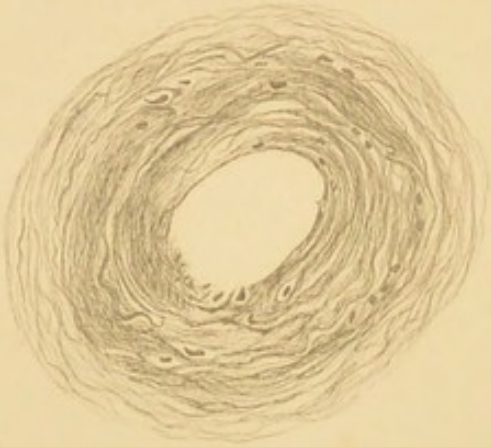

Fig. 3.

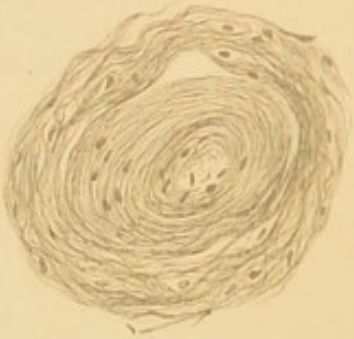

Fig. 4

Fig. 5.

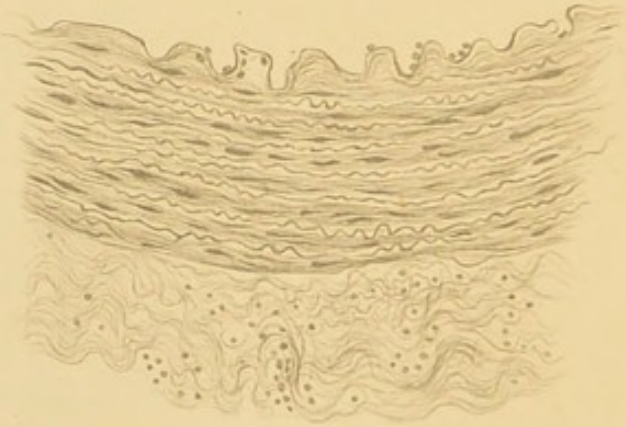

Fig. 6.

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DESCRIPTION OF PLATE I.

FIG. 1. Oblique section of an arteriole in the wall of the heart, from a case of granular kidney. The muscular and the external coat both hypertrophied.—× 100.

FIG. 2. Arteriole from the vagina of an ape. The muscular coat and the intima very thick, and so resembling a renal arteriole with hypertrophied walls.—× 200.

FIGS. 3, 4, 5 represent renal arterioles in different stages of atrophy subsequent to hypertrophy. L 265

FIG. 6. Transverse section of part of the wall of an artery about $\frac{1}{10}$ inch in diameter, from a recently killed animal, showing the three coats. In the middle coat the alternate layers of muscular and elastic tissue are well seen.—× 200.

Plate II.

Fig. 7.

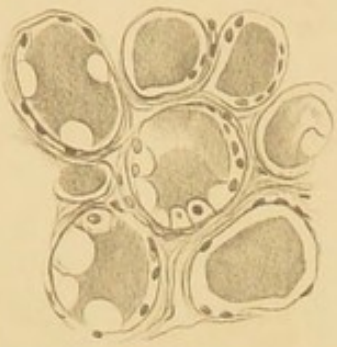

Fig. 8.

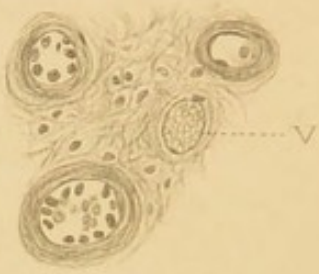

Fig. 9.

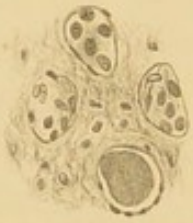

Fig. 10.

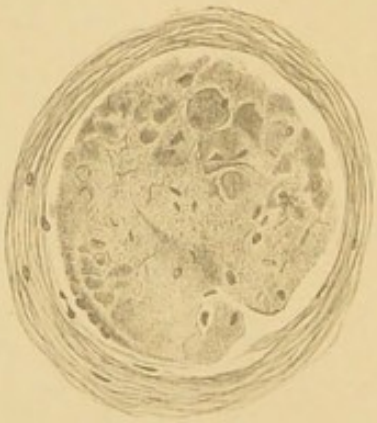

Fig. 11.

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DESCRIPTION OF PLATE II.

FIG. 7. Transverse section of a cerebral artery about $\frac{1}{8}$ inch in diameter, from a case of granular kidney; the walls irregularly thickened and the normal tissues replaced by fibroid degeneration, probably gouty.—× 20.

FIG. 8. Sections of tubes from a granular kidney; the tubes in close contact with each other and containing colloid material, some nuclei of epithelium, and round cells, some with a single nucleus.—× 200.

FIG. 9. Sections of tubes with thickened basement membrane. Two contain the nuclei of epithelium. In the interspace some scattered nuclei; *v*, transverse section of a vein containing blood.—× 200.

FIG. 10. Sections of wasted tubes. Three contain only nuclei of epithelium, one contains the colloid material; in the interspaces scattered nuclei but no fibroid tissue.—× 200.

FIG. 11. Malpighian body; the capsule thickened and the capillaries invaded and rendered indistinct by a colloid material.

These lithographic figures and the woodcut illustrations, Nos. 3, 4, 14, 15, are from accurate drawings of specimens under the microscope by Mrs. Danielsson, of 52 Beaumont Street.

No. 3.

London, 7, Great Marlborough Street, March, 1896.

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