A LECTURE ON THE VARIOUS FORMS OF RENAL TUBE-CASTS AND THEIR DIAGNOSTIC SIGNIFICANCE.

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GENTLEMEN,—The microscopic examination of the urine secreted during the different stages of the various forms of renal degeneration, which are usually included under the generic term "Bright's disease", affords evidence which, rightly interpreted, is of great value as to the morbid changes which are in progress within the kidney. This evidence is of a peculiarly interesting character, and is based upon the following facts: 1. That the glandular structure of the kidney is tubular; 2. That, while some structural changes are interstitial and intertubular, the most constant and important of the morbid processes are intratubular; 3. That portions of the various morbid products, after being moulded within the tubes, become loosened, and then, being detached and carried on by the secreted current of liquid, appear in the urine in the form of cylindrical casts of the tubes. 4. These tube-casts vary much in size and form, and in the materials of which they are composed; and they throw much light upon the condition of the tubes from which they have escaped.

Before proceeding to describe and interpret the various forms of tube-casts, let me give you one or two hints as to the best mode of finding and preserving them. If the casts be very numerous, they may be found at once by placing a drop of the urine under a power of 200 or 250 diameters; but, as a rule, it is desirable to put about four ounces of the urine into a conical glass, and allow it to stand for from twelve to twenty-four hours. At the end of that time, a sediment has usually formed; it may be only a slight or scanty cloud, or a more or less copious and dense deposit. If no sediment be visible, few or no tube-casts will be found even after the most careful and prolonged examination. A few drops of the sediment, taken up with a pipette, are then placed in a shallow cell made by cementing a thin ring of glass or metal on a glass slide; or a cell may be made of a ring of cement, such as Hollis's glue or Brunswick black. The cellful of liquid being covered by thin glass, and the excess of liquid removed by a cloth or blotting-paper, is now ready for examination. The examination is much facilitated by the use of the shallow cell. When the sediment is scanty, it is a waste of time to be searching for tube-casts in a fraction of a drop of the urine which alone can be retained between two flat pieces of glass.

And here let me say that the various forms of tube-casts may, with a little care, be preserved for an indefinite time. Some of the specimens which I shall presently show you were mounted more than a quarter of a century ago. I shall direct your attention especially to some specimens from which were made drawings to illustrate a paper of mine on the Forms and Stages of Bright's Disease, which was published in the forty-second volume of the *Medico-Chirurgical Transactions*. At page 161 of that volume you will see microscopic drawings of the various forms of tube-casts which were found at different stages of a prolonged case of Bright's disease. The specimens were mounted at different periods of the year 1856; and, if you compare them with the woodcuts, you will see that to this day they retain their characteristic appearance. These specimens of tube-casts, like most of those that I possess, have been preserved in pyroxylic spirit—one part of spirit to nine of water. The mixture of spirit and water becomes milky; but, after standing for some days, with an occasional shaking, it may be cleared by filtering through paper. I have lately been using a saturated solution of salicylic acid for the same purpose; and, so far as I can judge from a comparatively brief experience, it appears to answer well. It preserves the casts with little or no change of appearance.

In order to understand the significance of tube-casts, you have to bear in mind the structure of the kidney, with which I must assume that you are quite familiar. To suppose the contrary would be an insult to men studying in the school where, forty years ago, Bowman first demonstrated the structure of the Malpighian bodies. The basis of all tube-casts is an albumino-fibrous material derived from the blood, which, when it exists alone, forms a transparent structureless so-called "hyaline cast". "Hyaline casts" may be "small" or "large"; the

latter being about twice the diameter of the former, and having a more sharply defined outline. (Fig. 1.) What is the explanation of this

Fig. 1.—Large and Small Hyaline Casts $\times 200$.

difference of diameter? Not, as is sometimes carelessly asserted, the difference in the size of the tubes in which they have been moulded. The vast majority of the casts, both large and small, have been formed within the convoluted secreting tubes of the cortex, which are remarkable for their uniform size. The different diameter of the casts is explained by the fact that the small casts have been moulded within the lumen—the clear central canal—of convoluted tubes which retain their lining of glandular epithelium; while, on the other hand, the "large hyaline cast" has been formed within the basement-membrane of a tube the epithelial lining of which has been destroyed and displaced by the hyaline material of the cast. The large casts, therefore, point to a greater structural change within the tubes than is indicated by the small casts.

In some of the specimens which I have placed under the microscope, you may see a granular cylinder, composed of more or less altered epithelium, enclosed in a casing of the hyaline material, which, apparently having passed through the basement-membrane, has displaced and surrounded the epithelial lining of the tube. (Fig. 2.)

Fig. 2.—Granular Cast: enclosed within a Hyaline Cast $\times 200$.

Another interesting fact is, that many of the hyaline casts retain more or less of the convoluted form, which proves that, although in their exit from the kidney they have passed through the straight collecting tubes of the medullary cones, they were moulded in the tortuous secreting tubes of the cortex. (Fig. 3.)

Fig. 3.—Convoluted Hyaline Cast $\times 200$.

No doubt many of the long convoluted casts which, in sections of the cortex, may be seen filling the uriniferous tubes, become broken into short fragments during their passage through the straight tubes of the cones; and an indication of this process is often afforded by a fissure extending more or less deeply from the concave side of a curved

hyaline cast. The explanation of this is, that a convoluted cast, in passing through a straight collecting tube, has been partially torn asunder during the straightening process to which it has been subjected. I have hitherto spoken only of large and small hyaline casts. When, as frequently happens, in cases of acute congestion of the kidney, blood escapes from ruptured Malpighian capillaries into the uriniferous tubes, some of the blood coagulates within the lumen of the tubes, and afterwards appears in the urine in the form of "blood-casts". These casts have the same diameter as the "small hyaline casts".

But the most constant and characteristic structural change resulting from the acute renal disease, which is excited by scarlet fever, by exposure to cold and wet, or other well known exciting causes, consists in a rapid new formation and desquamation of the glandular epithelium of the convoluted tubes. This is the essential feature of the disease, which I originally designated "acute desquamative nephritis". The desquamated gland-cells become entangled in the tube-casts, which we know as "epithelial casts."

All the forms of tube-cast which I have mentioned—namely, the "small and large hyaline casts," "blood-casts," and "epithelial casts" may be seen in varying proportions in every typical case of acute desquamative nephritis.

During the progress of acute nephritis, it not unfrequently happens that some of the exudation-products undergo an oily transformation, and oil accumulates in the gland-cells. This change is indicated by the appearance of "oily casts" and "oily cells" in the urine (Fig. 4).

Fig. 4.—Oily Casts and Cells $\times 200$.

A few oily casts and cells mingled with the other casts which I have described have no specially unfavourable significance; but when, after albuminuria has continued for several weeks or months, the oily casts and cells preponderate, or even entirely replace the other forms, there will be reason to fear that the kidney is undergoing an incurable fatty degeneration; and, if death occur at this stage, the kidney will be found enlarged and pale, while, through its cortical portion, yellow granules of fatty degeneration will be found scattered. This constitutes the large, white, granular, fat kidney.

When acute desquamative nephritis has passed into a chronic state, there may, for a number of years, be little or no disorder of the general health; but the urine is persistently more or less albuminous. Tube-casts may be entirely absent, or there may be a light cloudy deposit containing small hyaline casts with an occasional oily cast, or oil-containing cell. As the disease makes progress, the urine gradually loses its normal sherry tint, and at length becomes more or less colourless. If, at the same time, the deposit become more dense and copious, and contain large granular and large hyaline casts, indicating extensive destruction of the uriniferous gland-cells, we have, in these appearances, evidence that a process of granular contraction has begun in the cortical portion of the kidney; and the gravity of the prognosis is greater in proportion to the amount of this microscopic sediment in the urine.

Glomerulo-Nephritis.—The acute renal disease which results from scarlet fever has not always the character of desquamative tubular nephritis. There is a form of nephritis to which attention was first directed by Dr. Klebs, under the name of "glomerulo-nephritis". In this form of disease, the chief anatomical change consists in an accumulation of leucocytes within the Malpighian capsules. Long before the publication of Klebs's observations, I had noticed the occasional appearance in the urine of small casts entangling leucocytes (Fig. 5). I have here a specimen of such casts, mounted in 1856. The case was fatal, and I have preserved a section of the kidney; in which may be seen the Malpighian capsules rendered opaque by the accumulated leucocytes. I confess, however, that, until I became acquainted with the observations of Klebs, I did not appreciate the full significance of these appearances.

In my *Lectures on Bright's Disease*, published in 1873, I have suggested (p. 35) what I have no doubt is the true explanation of the sources of the "white cell casts", or, as I then called them, "exudation-cell casts"—namely, that the leucocytes or white blood-cells, having

migrated through the walls of the Malpighian capillaries, subsequently became moulded into small cylindrical casts within the central canals of the convoluted tubes. The white cell-casts are the diagnostic indications of the existence of glomerulo-nephritis, and they are the complement and counterpart of the anatomical changes within the Malpighian capsules.

Fig. 5.—White Cell-Casts $\times 200$.

Although the two forms of disease here referred to—namely, tubular desquamative nephritis and glomerulo-nephritis—may exist apart, yet I am convinced, from clinical observation, and in particular from microscopic examination of the urine, that they are often combined in various degrees in the same subject. The epithelial and other forms of tube-cast which I have described as diagnostic of desquamative tubular nephritis being frequently associated, in varying proportions, with the white cell casts of glomerulo-nephritis.

The Small Red Granular Kidney.—The urine secreted by the small red granular, or, as it is sometimes called, the gouty kidney, is usually copious, of low specific gravity, and more or less albuminous, though the albumen is not rarely scanty, and at some periods of the disease even entirely absent. The absence of albumen, however, in undoubted cases of granular kidney, is rare, and there is no evidence to show that any case of the disease has passed through all its stages to a fatal termination without the more or less frequent and copious appearance of albumen in the urine. The microscopic evidence of the existence of the small red kidney consists in the appearance of "granular casts", containing epithelial cells from the uriniferous tubes in various stages of disintegration. All so-called granular casts, however, are not composed of disintegrated epithelium. Blood may become disintegrated within the tubes, and appear in the urine as granular blood-casts, distinguished from granular epithelial casts by their reddish-brown colour, and often by their containing some entire blood-corpuscles. So, again, a disintegrated hyaline cast may assume a granular appearance; but, by a comparison with other casts associated with them, and noting the various grades of change, we trace them to their true source.

The presence of granular epithelial casts and scattered epithelial debris is evidence that a process of epithelial degeneration and disintegration is going on in the kidney. In the earlier stages of the disease, the granular casts may be occasionally absent, but as the disease makes progress, they may always be found, if carefully looked for; and in the later stages, the granular casts are often found associated with large hyaline casts in variable proportions. Not only is the contracting form of renal disease indicated by the microscopic appearances of the sediment, but the number of granular and large hyaline casts, and the amount of epithelial debris indicate the rate at which the disease is progressing. The more copious this sediment, the more rapid is the destruction of the gland-cells and the consequent atrophy and disorganisation of the kidney.

Lardaceous Degeneration of the Kidney.—There are no forms of tube-cast which are specially significant of lardaceous degeneration of the kidney. The diagnosis of this disease has to be based upon a consideration of the general history of the case rather than upon the microscopic appearances in the urine. The urine may be copious and clear, and deposit no sediment; and in the earlier stages of the disease tube-casts are never numerous. In most cases, however, a light cloud is deposited, and in this may be found some small hyaline casts, some casts finely granular, and occasionally some oily casts and cells. In the advanced stage of the disease, when atrophy and contraction of the kidney are in progress, the urinary sediment may be copious and dense, containing numerous dark granular and large hyaline casts, similar to those which I have described as occurring when a large white or a granular fat kidney has reached an advanced stage, and is undergoing atrophy and granular contraction.

You may probably have heard or read that more than one recent writer on renal pathology has asserted that no tube-casts can escape from the convoluted tubes of the cortex of the kidney. This assertion is based upon the assumption that all the convoluted tubes pass into the so-called Henle's loops, which are supposed to be too narrow to permit the passage of tube-casts. This anatomical assumption I believe to be erroneous.

It is at any rate quite certain that the great majority of tube-casts which appear in the urine have been moulded within the convoluted tubes of the cortex. The casts which evidently have this origin are: 1. The oily casts, the fatty infiltration being as a rule confined to the glandular epithelium of the convoluted tubes; 2. The small white-cell casts, containing the leucocytes, which can have no other source than that of migration through the walls of the Malpighian capillaries; 3. Blood-casts, the result of hæmorrhage from the Malpighian capillaries into the commencement of the convoluted tubes; 4. Those large hyaline casts which after their escape with the urine, retain the convoluted form, clearly indicating their source in the tortuous tubes of the cortex. 5. The epithelial casts, which contain numerous cells, having all the characters of the glandular epithelium of the convoluted tubes. These unquestionable facts are clearly inconsistent with the theoretical assumption that no casts from the cortical portion of the kidney can escape, and appear in the urine.

I trust that I have succeeded in convincing you that the structure of the various forms of tube-cast which appear in the urine is both interesting and of high practical value. And now I must remind you that, in order to obtain trustworthy data from a microscopical examination of the urine, your observations of the phenomena must be exact, and your interpretation cautious and rational. You must accurately discriminate between one form of tube-cast and another, and you must avoid the not very unusual error of mistaking for tube-casts appearances somewhat resembling them, which are due to the presence of foreign bodies in the urine. I have here a specimen which was given to me by an enthusiastic but inexperienced microscopist, to illustrate his supposed discovery of brightly and variously coloured tube-casts, some being red, others yellow, and others again green. These supposed tube-casts, as you will see, are in reality coloured fibres of wool, no doubt having their source in floating dust from a carpet. An unpractised observer often mistakes a fibre of cotton or a hair for a tube-cast.

I was once invited to confirm the diagnosis of cancer of the kidney which had been very confidently inferred by two experienced practitioners from the microscopical appearances in the urine. On looking at the specimen which had been prepared for my inspection, I found that the supposed cancerous products from the kidney were obviously grains of starch, which, on inquiry, were traced to their source in the application of violet powder to the external genitals of a female patient. The patient's recovery afforded the crowning proof of the absence of cancer.

A very moderate amount of care and study will enable you to avoid such gross errors of observation and interpretation as those to which I have referred.

In conclusion, let me impress upon you the importance of avoiding the not uncommon error of basing your diagnosis, your prognosis, or your indications for treatment, too exclusively upon one kind of evidence. After all that I have said and written upon this subject, I shall not be suspected of attaching too little importance to the information to be derived from a careful microscopical and chemical examination of the urine. The importance of this inquiry, in all cases of renal disease, can scarcely be overestimated. On the other hand, information of the highest practical value, with regard to the form and the stage, and the gravity of the renal disease, is to be derived from various other sources—such as, for example, the presence or absence of dropsy; the colour and expression of the face; the state of the vision and the ophthalmoscopic appearances of the fundus of the eye; the odour of the breath; the presence of such nervous phenomena as headache, giddiness, twitching or painful cramp of certain muscles; the condition of the skin, which, in the advanced stages of the various forms of Bright's disease, is almost invariably dry and harsh, and with difficulty forced into a state of active secretion; and last, but not least, the condition of the circulation, as indicated by the degree of arterial tension, and the impulse and sounds of the heart.

The practice of medicine, like the art of war, is, in a greater or less degree, a succession of mistakes—the best generals and practitioners being those who make the fewest mistakes; and the surest way to avoid error, whether in war or in medicine, or in any other art, is by a diligent endeavour to base every scientific or theoretical opinion, and every practical doctrine, upon the widest and most exact observation of all the facts which have relation to the subject in hand.

The unscientific absurdity and the practical evils of a narrow and exclusive specialism, can scarcely be better shown than by the study of the various forms of renal degeneration, whose influence upon the general system is so wide and far reaching, that, during their progress, almost every tissue and organ and function of the body may suffer more or less perversion and derangement; and so typical and characteristic are some of these secondary results of renal disease, that, in one case,

the ophthalmoscope; in another, the finger on the full and tense radial artery; and in another, the hand or the stethoscope over the strongly heaving hypertrophied heart, has alone sufficed for the diagnosis of advanced degeneration of the kidney.

SELECTIONS FROM CLINICAL LECTURES,

Delivered at the London Hospital.

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PAPILLARY GROWTHS IN THE LEG PRECEDING CANCER.

WE had, some time ago, through the kindness of Dr. Stephen Mackenzie, several opportunities of seeing a man who has some very peculiar growths on the lower part of one leg. There are several patches of a papillary growth close together, and almost confluent, a quarter of an inch or more in height. On their surface, the papillary outgrowths are covered by a dirty scab; but if we detach or break this, you can easily separate the wart-like growths from each other, and put them apart in long rows, like standing corn. They do not readily bleed, and the skin from which they grow is somewhat thickened. The main patch is over the shin, in front of the lower third of the leg, and is nearly as large as the palm of the hand; but near it are several much smaller ones. The first stage of the condition is a thickened and rough papule, not unlike a spot of psoriasis, but with more evidence of growth. Our patient is a man of near 50, and he has had the condition for two or three years. It gives him no trouble. He has no enlarged glands.

I do not think that there can be much hesitation in considering that the disease as a variety of papilloma which, if not actually cancerous at present, is in a fair way to become so. At any time we might find the glands enlarged, or that the patch had begun to ulcerate. It is mainly in the absence of any ulceration that the picture of epithelioma is as yet incomplete. There is no telling how long or how short may be the period during which its appearance will be delayed. I have urged the man to at once submit to radical treatment, that is, to have the growths freely destroyed by chloride of zinc paste.

Dr. Mackenzie's patient shows an extreme condition of what, in lesser forms, I have often seen before. An old man, aged 74, came to us at the Hospital for Skin-Diseases, last week, who had exactly the same thing, but in smaller areas and with less elevation. They had been present two years, and, excepting that they itched excessively, gave him no trouble. In him, one of the patches was at the back of the leg; most of them, however, being in the usual position—over the shin. I will ask you to note, in connection with this fact, that the patches are almost always multiple—a chief one and several smaller near to it. Although I ask you to believe that this disease is really a close ally of cancer, yet I do not know that I can quote any complete case in which I have watched patches which began as I have described, and progressed to an undoubtedly cancerous termination. But I have seen several which were cancerous, in which there was good reason to believe that the beginning had been like them. It is only in the legs of aged people that we see such growths; and the liability to them seems to begin at the cancerous time of life. Often some local irritation, eczema, etc., precedes their formation. Not unfrequently, during periods of some years, the patches remain without warty or papillary outgrowth, simply hard rough patches, well circumscribed, and showing on the surface the little points or buds from which future growth is to take place. In this stage they resemble condylomata, excepting in their hardness and roughness. Often, however, they are not round, but in long streaks and very irregular. Probably they are, for the skin of the leg, what the rodent cancer is for the upper part of the face—the form of malignant action which it is most prone to take on. I have not often seen them on other parts of the body.

ON THE PECULIAR CONDITIONS ASSUMED BY MALIGNANT DISEASE OF THE SKIN IN DIFFERENT REGIONS.

You are aware that it is a doctrine upon which I often insist, that certain differences in the clinical characters of malignant disease of the skin are to be observed in relation with the different surface regions of the body. The upper part of the face grows rodent cancer; the lips, ears,