LECTURES

ON THE

PATHOLOGY, DIAGNOSIS, AND TREATMENT OF BRIGHT'S DISEASE.

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

Physician to King's College Hospital; Professor of Medicine in King's College, London; etc.

LECTURE V.—CHRONIC BRIGHT'S DISEASE, WITH A LARDACEOUS OR WAXY KIDNEY.

General History.—*Virchow's erroneous Theory.*—*Clinical History and Symptoms.*—*Minute Anatomy and Pathology of the Kidney.*—*Its Relation to Continued and Profuse Suppuration.*—*Hypertrophy of the Heart.*—*Diagnosis.*—*Prognosis.*—*Hæmaturia in Chronic Bright's Disease.*

THERE are cases of chronic Bright's disease associated with kidneys which are usually enlarged, anæmic, pale, and wax-like; thus resembling in some respects the cases which I described to you in my last lecture. But the form of disease to which I now invite your attention has for the most part a peculiar and distinctive clinical history; and the anatomical condition of the kidney is in some respects different from that of the ordinary large white kidney.

General History.—The subjects of this form of disease have usually been strumous or otherwise cachectic before the onset of the renal degeneration. In some cases, there has been strumous disease of a joint or of one or more bones, with long continued suppuration; in others, there are the symptoms of phthisis. In a large proportion of cases, there is a history of constitutional syphilis, with resulting cachexia. In some cases cancer, in others dysentery, in others habitual intemperance, in others, again, long continued albuminuria following upon acute Bright's disease, has led to the cachexia out of which this form of renal disease has sprung. One of the earliest symptoms of the disease is a copious flow of urine, at first perhaps not albuminous, but subsequently more or less impregnated with albumen. Another common symptom is profuse and obstinate diarrhoea. Dropsy, more or less general, usually occurs; but it is not so constant or so prominent a symptom as in the class of cases which I described in my last lecture as sequelæ of acute Bright's disease. When at length the patient dies, sometimes from uræmia, but more frequently from exhaustion, the kidneys are found in a state which has been called "lardaceous" or "waxy degeneration". The gland is usually enlarged, sometimes very much so. In one of my own cases, the two kidneys weighed twenty-eight ounces. Dr. Dickinson in one case found their combined weight thirty-three ounces. The surface of the kidney is smooth and pale; the texture of the anæmic and thickened cortex is firm, and has the semi-translucent appearance of white beeswax; while the cones retain their normal colour, vascularity, and size. The cut surface presents numerous glistening points, due to the altered Malpighian capillaries. In some cases, minute yellow fat-granulations are scattered through the cortex. This is the large smooth lardaceous kidney; and one of its most remarkable and distinctive features is, that in the majority of cases it is associated with an analogous condition of the liver or spleen, or of both. In a certain proportion of cases, a stage of atrophy follows upon that of enlargement; the cortical substance wastes, and coarse granulations appear on the surface. This is the "contracted" or "granular lardaceous kidney". Such a kidney is represented in Figs. 1 and 2 of Dr. Bright's third Plate. It is remarkable that Dr. Bright's plates contain no illustration of the small red granular kidney, whose history I gave you in my third lecture.

Before entering upon a minute description of the kidneys, it will be well to give a brief history of the disease and of the speculative doctrines to which it has given rise. Virchow is the author of two theories regarding this disease. The one theory is, that the blood-vessels are the primary seat of the degenerative changes; and the other is, that the morbid deposit is of the nature of starch or vegetable cellulose; and he therefore calls the disease "amyloid degeneration". I shall presently show you that the first theory is erroneous; and the second is now universally admitted to be so. The term "amyloid" was suggested by a supposed chemical resemblance between the morbid deposit and vegetable cellulose or starch, as shown by the staining with a solution of iodine; but careful analyses by various competent chemists have shown that the material has essentially the same compo-

sition as the protein compounds, and that it is of an albuminous or fibrinous nature.

It is very desirable that the term amyloid, which is based upon an erroneous chemical theory, should be discontinued; and that the term "lardaceous", recommended by a Committee of the Pathological Society (vol. xxii, p. 2), should be adopted. The term lardaceous means no more than that the disease has the appearance of bacon fat (*lardum*, the fat of bacon); as the term "waxy" is based upon its resemblance to wax. These names, thus understood, imply no theory as to the composition of the morbid product, and are, therefore, not misleading, as the term amyloid unquestionably is.

Clinical History and Symptoms.—The clinical history of this disease has been carefully investigated; and we are indebted to Dr. Grainger Stewart for insisting upon the fact that a copious flow of urine, of pale colour and of low specific gravity, is one of the earliest and most constant symptoms of this form of degeneration. The urine at first may contain no albumen; but gradually it becomes albuminous, and often copiously albuminous. When a patient, whose strength has been reduced by a protracted and exhausting disease, begins to pass urine in large amount and of low density, so that his nights are disturbed by frequent calls to empty the bladder and to quench his thirst, we may anticipate that his kidneys are about to undergo the degenerative changes which we are now discussing. In the absence of sugar and albumen, it may for a time be a question whether the disease is diabetes insipidus. The appearance of albumen points at once to renal degeneration. The amount of urine secreted daily usually ranges from 50 to 100 ounces or more. The colour is pale, and the specific gravity varies from 1005 to 1015. The urine may be clear, and deposit no sediment; so that for days and even weeks together no tube-casts are visible; and, in the earlier stages of the disease, tube-casts are never numerous. In most cases, however, a light cloud collects at the bottom of the conical glass; and in this cloud we find some small hyaline casts, some casts finely granular, and occasionally some hyaline casts containing oil either in scattered globules or in cells. In the advanced stage of the disease, when atrophy and contraction of the kidney are in progress, the sediment in the urine may be copious and dense; and it will be found to contain numerous large-sized granular and hyaline casts, exactly similar to those which I described as occurring when the large white kidney has reached the third stage, and is undergoing atrophy and contraction (see *ante*, Figs. 25, 26, and 27). As the disease advances, the patient's weakness increases; his breath is short on exertion; his countenance is pallid or sallow; the feet, ankles, and legs become oedematous. In many cases, the liver and the spleen are seen and felt to be more or less enlarged; and the abdomen is sometimes much distended by fluid. The disease often has a very chronic course, extending over a period of many months or even years. There may sometimes be a temporary amendment; but in the majority of cases the symptoms gradually become worse, until at length the patient sinks, either from the direct effects of the renal disease, or from one or other of the associated maladies. The immediate cause of death may be dropsical effusion within the chest, in the pleura or pericardium, or in both. In other cases, the patient dies exhausted by diarrhoea, with or without vomiting—the result, probably, of blood-deterioration and the elimination of morbid materials through the mucous membrane of the alimentary canal. In some instances, the immediate cause of death is an attack of convulsions or coma. Cerebral symptoms of uræmic origin are, however, less frequent results of this than of other forms of chronic Bright's disease. The retina is rarely if ever affected. Inflammatory complications are of common occurrence. Of these, pneumonia is the most frequent; next to this, inflammation of the serous membranes, especially of the pleura. The pericardium and the peritoneum are more rarely the seat of inflammation.

In many cases, death results, not from the direct consequences of the renal degeneration, but from some associated constitutional disease or cachexia. Thus phthisis, or protracted suppuration, with or without disease of the bones or joints, or some form of constitutional syphilis, may be the immediate cause of death.

In the advanced stages of the disease, there is extreme anæmia and pallor of the skin; the blood contains much less than its due proportion of hæmoglobin and albumen, and in some cases an excess of urea.

Hæmorrhage from one or more mucous membranes, more especially from that of the nose, is an occasional occurrence in the advanced stages of the disease.

The Minute Anatomy and Pathology of the Lardaceous Kidney.—Most recent writers on renal pathology accept Virchow's theoretical interpretation of this disease, and assume that the first pathological change consists in thickening and degeneration of the walls of the minute arteries and Malpighian capillaries. In consequence of this degene-

ration, we are told, albuminous and fibrinous materials transude through the walls of the vessels, and infiltrate the tissues of the kidney; and this is supposed to explain the structural changes in the gland. It has also been suggested that the copious secretion of urine in the early stage of the disease is a result and an indication of paralysis and dilatation of the minute renal arteries, consequent on degeneration of their walls. I find this theory inconsistent with anatomical facts, and therefore I reject it entirely. For a number of years I have most carefully studied the condition of the renal blood-vessels in all forms and stages of Bright's disease. My discovery of hypertrophy of the muscular walls of the arteries was published in the year 1850 (*Med.-Chir. Trans.*, vol. xxxiii), some years before the publication of Virchow's theory of amyloid degeneration. I soon learnt to distinguish muscular hypertrophy from lardaceous and fatty degeneration of the arterial walls; and I have carefully noted the microscopic appearances in a large number of diseased kidneys. The result is that, while I have not met with a single case in which thickening of the renal blood-vessels in any form was unassociated with extensive changes in the secreting tissue of the kidney, I have examined many kidneys in an advanced stage of lardaceous disease with only incipient degeneration of the blood-vessels. For example, I have before referred to one case in which the two kidneys weighed twenty-eight ounces. The patient at the time of his death was twenty-one years of age. Since the age of three, he had suffered from disease of the hip, with purulent discharge from several openings about the joint. For ten or eleven years there had been more or less dropsy, and for several months the dropsy had been general. The clinical history, the character of the urine, and the appearance of the kidneys, were those of a typical case of lardaceous degeneration of the kidney; yet the Malpighian capillaries and the arteries in these greatly enlarged, pale, and wax-like kidney, after the long duration of the symptoms, were only moderately thickened. The gland had increased to nearly three times its normal weight, while the vascular changes were in an incipient stage. The increased size of the gland was not such as could be explained by a mere infiltration of fibrinous material; but the enlargement was the result mainly of an actual hypertrophy of the glandular tissue, precisely similar to that which I described in my last lecture as occurring in cases of the large white kidney. Most of the tubes were enlarged, and their epithelium was opaque from "cloudy swelling". In some, the cells were in a state of fatty degeneration; and some tubes contained fibrinous coagula precisely similar to the large hyaline casts which had appeared in the urine during life. In some cases, more especially when the disease has gone on into the stage of atrophy and contraction, the gland-cells have undergone more general and extensive degeneration. Numerous small yellow spots visible by the naked eye, when present, indicate the situation of tubes whose contents have undergone fatty degeneration (see *ante*, Fig. 18); while other tubes were filled with unorganised fibrine, which may sometimes be squeezed out of them in the form of large hyaline casts. The basement-membrane, both in the cortex and in the cones, sometimes appears thickened and hyaline; and occasionally the tubular structure is rendered indistinct by an unorganised intertubular effusion. The Malpighian capillaries are thickened, opaque, glistening, and wax-like. (Fig. 30.) Some of the afferent arteries appear

Fig. 30.—Malpighian Capillaries, with Opaque Glistening Wax-like Walls. The Capsule somewhat thickened.— $\times 200$.

quite normal, others thickened by muscular hypertrophy; but the greater number appear thick, more or less homogeneous, and wax-like; their muscular structure being concealed apparently by an interstitial fibrinous infiltration. (See Fig. 31.) The straight arteries in the

Fig. 31.—Lardaceous Infiltration of its Walls.— $\times 200$.

cones sometimes present the same appearance of wax-like degeneration. If we now add to the specimen a drop or two of diluted liquor potassæ (one part of solution of potash in ten of water), the walls of the waxy vessels are rendered transparent; so that the red blood-corpuscles become visible through the thickened Malpighian capillaries, and the muscular fibres of the minute arteries are rendered quite distinct. The weak alkali has a solvent action upon the infiltrated fibrinous material, and thus to some extent brings into view the normal structure of the arterial walls. The canals of the afferent arteries may sometimes be seen irregularly dilated. In some of the arterial canals, a collection of oil-globules shows that the circulation has ceased some time before death. (Fig. 32.) Oil-globules may often be seen in the canals and in the

Fig. 32.—An Artery, with Lardaceous Infiltration of its Walls and collections of Oil-globules in the Canal, which is somewhat irregularly dilated.— $\times 200$.

walls of the Malpighian capillaries—less frequently within the intertubular capillaries. I have never seen thickening of the walls of the intertubular capillaries. Thickening of the basement-membrane often gives an appearance of intertubular thickening. When fatty granulations are visible to the naked eye, their microscopic appearances are identical with those which I have before described in the granular fat kidney.

In my last lecture, I told you that the Malpighian capillaries and the walls of the minute arteries in some large white kidneys are thickened, homogeneous, and wax-like. The vessels in these cases have undergone precisely the same change as those in the lardaceous kidney. In fact, the large white kidney, which is found associated with chronic albuminuria following upon acute Bright's disease, and the lardaceous kidney, which occurs in connexion with chronic cachexia, have many points of contact and relationship; and the two forms of disease merge into each other by imperceptible gradations. Chronic albuminuria is generally admitted to be one of the causes of lardaceous degeneration of the kidney.

All writers on the lardaceous kidney agree in stating that the primary cause of the renal degeneration is a morbid condition of the blood. In this opinion I concur; and I believe that some morbid material in the blood, acting upon the secreting tissues of the kidney, is the cause of the copious secretion of urine in the earlier stages of the disease, and of the glandular hypertrophy which gradually supervenes during the progress of the malady. It is probable that the unknown morbid material in the blood has a diuretic influence upon the kidney, analogous to that which grape-sugar is known to have in cases of saccharine diabetes. We do not attempt to explain the diabetic urinary flux by the anatomical condition of the kidney; neither can we thus explain the copious secretion of urine which precedes lardaceous degeneration. I say *precedes* the degeneration; for my observations have convinced me that, while in the earlier stages of the disease the arterial walls are quite normal, at a later period they may become hypertrophied; and later still, either with or without previous hypertrophy, they become infiltrated with fibrinous material, and assume the homogeneous waxy appearance. The Malpighian capillaries in every case of albuminuria have a more or less abnormal appearance. I told you in my second lecture that, after death from acute Bright's disease, the walls of the Malpighian capillaries are opaque and granular. In all cases of chronic albuminuria, the same capillaries are thickened; and, when the transudation of albumen has been copious and long continued, the capillary walls always assume an opaque, glistening, wax-like appearance. The state of the Malpighian capillaries in the large white kidney is not distinguishable from that of the same vessels in the lardaceous kidney, either by microscopic examination or by any chemical test with which I am acquainted. The test which is usually applied is a weak solution of iodine. The thickened arteries and Malpighian capillaries take the reddish-brown stain much more deeply than the other tissues; and the stained vessels consequently stand out in strong contrast with the pale, waxy, glandular structure. This iodine test, applied to the large white smooth kidney, often stains the vessels as

deeply as when applied to the lardaceous kidney, and thus affords additional evidence of the close relationship between the two forms of disease. I cannot but think that too much importance has been attached to the iodine test, while too little attention has been given to the minute structural changes in the kidney and their physiological interpretation.

Dr. Dickinson attributes so much influence to *suppuration* as causative of lardaceous degeneration, that he proposes to call the disease "depurative", using the word in a sense different from that in which it is commonly understood. Analyses of the morbid material, especially in the liver, have led him to the conclusion that it consists of partially dealcalised fibrine. He supposes that copious suppuration, by lessening the albumen and alkalies in the blood, causes a deposit of dealcalised fibrine in various tissues and organs. It seems not improbable that the diminished alkaliescence of the waxy liver may be explained by the comparatively small proportion of alkaline blood which it contains. The liver-cells are infiltrated with, and in part replaced by, fibrinous material; while the vessels are compressed and anæmic. There is no apparent difference between the fibrinous exudation within the tubes of a lardaceous kidney and that which is found in the tubes of a large white kidney, the result of acute Bright's disease passing into a chronic form. Our knowledge of animal chemistry is as yet too elementary to enable us to give a chemical explanation of pathological changes so complex as those which we are now discussing; and, although the lardaceous disease is very frequently associated with suppuration, yet this is far from being constant. The renal degeneration occurs in only a small proportion of cases in which there has been profuse and protracted suppuration; and, on the other hand, the lardaceous form of renal degeneration not unfrequently occurs unassociated with a history of purulent discharges. Dr. Grainger Stewart states that in only six out of eighteen cases which he had himself carefully investigated, was there a history of suppuration. Obviously there is not that constant and close relationship between suppuration and lardaceous degeneration which justifies the application of the ambiguous term "depurative" to this form of renal disease. It is probable that the deterioration of blood which results from long continued profuse suppuration is due rather to the drain of albumen than to the loss of alkaline salts; and so it is intelligible that chronic suppuration and chronic albuminuria may bring about a similar condition of cachexia and malnutrition.

Hypertrophy of the Heart, unassociated with disease of the valves or of the large arteries, rarely occurs, except in the cases which have passed on into the stage of atrophy. The explanation which I gave in my last lecture of the comparative infrequency of hypertrophy of the left ventricle in cases of large white kidney, is applicable here also. There is more of hydræmia than of uræmia associated with the lardaceous kidney; and the minute arteries offer little or no resistance to the passage of this watery blood. In addition, we have to take into consideration the fact that the walls of the minute arteries in various tissues and organs usually undergo degenerative changes, whereby their contractile power is impaired. The degeneration of the blood-vessels is of common occurrence in the mucous membrane of the intestines, and the change is rendered conspicuous by the iodine test. The absence of abnormal contraction in the terminal arteries explains the absence of the cardiac hypertrophy which ordinarily results from long continued and excessive arterial resistance.

Diagnosis.—You will probably have inferred, from what I have said of the close relationship between the "large white kidney" and the "lardaceous kidney", that it is often difficult to distinguish one from the other, and that the distinction has but little practical value. Even when you have the diseased organ before you, you may sometimes be in doubt whether to call it simply a "large white kidney", or to designate it "lardaceous". Obviously, then, it must sometimes be impossible to make the distinction during the lifetime of the patient. When there has been a copious secretion of urine, which for a time was free from albumen, but later has become copiously albuminous; when a copious secretion of pale albuminous urine, of low specific gravity, is associated with more or less general dropsy; when these symptoms have come on gradually and insidiously in a subject who has been suffering from an exhausting disease, such as phthisis, disease of the bones or joints, or cachexia resulting from cancer or constitutional syphilis, we may expect to find lardaceous degeneration. The probability of this will be much increased, if the liver or spleen, or both these organs, be found enlarged and indurated. A lardaceous kidney may sometimes attain a sufficient size to be palpable in the lumbar region. The tube-casts, when present, are essentially the same in the two forms of disease; and in particular the large hyaline and granular casts (Figs. 26 and 27), which appear in the advanced stages of both classes of cases, announce that atrophic changes are in progress; while the

amount of sediment having these microscopic characters indicates the rate at which the destructive changes are proceeding.

Prognosis.—Although the history of this form of disease not unfrequently extends over a period of several years, as in the somewhat exceptional case to which I just now referred, yet the prognosis is, as a rule, very unfavourable—for the obvious reason, that not only is the renal disease often associated with serious structural change in other organs, but, resulting as it does from a grave constitutional cachexia, its causes are continually operating, and, as a rule, they are but little amenable to treatment. There may be occasional pauses in the progress of the disease, and even periods of temporary amendment; but the usual course of the malady is one of steady progress towards a fatal termination. The end is often hastened by an exhausting diarrhoea, by a copious dropsical or inflammatory effusion into the chest or abdomen, or by inflammation and sloughing of the dropsical legs.

Hæmaturia in Chronic Bright's Disease.—In conclusion, I wish to direct your attention to a possible source of fallacy resulting from the occasional appearance of blood-tinged urine in the advanced stage of this and of other forms of chronic Bright's disease. Dark-coloured, smoky, more or less blood-coloured urine, is of frequent occurrence in cases of acute Bright's disease; it is rare in the advanced stages of any of the three forms of chronic disease which I have described, but it does occasionally happen; and the appearance of hæmaturia might possibly mislead you in your estimate of the stage and gravity of the renal disease.

During the progress of the various forms of chronic Bright's disease, the walls of the Malpighian capillaries become thickened, and therefore probably less liable to be ruptured. In many cases, too, the muscular walls of the minute arteries are more or less hypertrophied; and the effect of this is to lessen the pressure upon the Malpighian capillaries and the risk of their rupture. This appears to be the explanation of the undoubted fact that the pale urine of low specific gravity which is secreted by kidneys in an advanced stage of degeneration, is rarely tinged with blood. This rule, however, is not without exceptions. In the advanced stage of all forms of chronic Bright's disease, the blood becomes much deteriorated—partly, as we have seen, by the loss of its normal constituents; partly by the retention of urinary excreta. In some tissues, too, the minute arteries and capillaries may undergo degenerative changes which increase their liability to rupture. There is consequently a tendency to hæmorrhage from various mucous surfaces—from the nose, the lungs, the stomach and intestines, from the uterus, and sometimes from the mucous membrane of the bladder and the pelvis of the kidney. Hæmorrhage from the bladder, or from the pelvis of the kidney, may give the urine the dark colour and the blood-tinged appearance which it often has in cases of acute Bright's disease, when blood escapes from the substance of the kidney. You may come to a right judgment in these cases by a careful consideration of the past history, together with a close inspection of the urine. You will probably find that there are no blood-casts of the tubes, as there usually are when the substance of the kidney is the source of the bleeding. You may find some of those forms of tube-cast which point to the existence of chronic rather than recent acute disease: for instance, oily casts or large granular and large hyaline casts (Figs. 25, 26, and 27). You may also find that the urine, when, after standing for a time, it has deposited the blood, presents the pale colour which is indicative of chronic disease in an advanced stage. Many years ago, my friend Mr. James Salter sent me the notes of a case of *purpura* in which there had been profuse hæmaturia. The kidneys had been the seat of chronic Bright's disease; they were enlarged, anæmic, and had some cysts on their surface. The mucous membrane of the calyces, infundibula, and pelvis, was intensely congested, and chocolate-coloured with ecchymosis. There was a striking contrast and a sharp line of demarcation between the pale mamillæ and the dark ecchymosed calyces. It is probable that the absence of hæmorrhage into the substance of the kidney was due to the fact that the walls of the minute arteries and those of the Malpighian capillaries had become thickened during the progress of the chronic degeneration of the kidney which had long preceded the appearance of the purpura. This case affords a good illustration of the fact that hæmaturia, the result of blood-deterioration, may have its source in the pelvis, and not in the substance of the kidney. A microscopic examination of this patient's urine had discovered no tube-casts. None of the blood had been moulded within the uriniferous tubes, because none had escaped from the Malpighian capillaries.

LORD HENRY SEYMOUR'S BEQUEST.—At the Rolls Chambers, on the 1st instant, a further sum of £83, to be paid to eighty-three London charities, making altogether £665 to each, or more than £56,000 out of the estate, was ordered.