THE LUMLEIAN LECTURES ON BRIGHT'S DISEASE.

Delivered before the College of Physicians.

By REGINALD SOUTHEY, M.D.Oxon., F.R.C.P.,
Physician and Lecturer on Clinical and Forensic Medicine at St. Bartholomew's Hospital.

LECTURE II.—PART II.

IN 1879, a most important memoir was published in Volkmann's *Klin. Vorträge*. Nos. 162, 163, p. 1411, by Carl Weigert. The writer seeks to settle the vexed question of the varieties of Bright's disease, its unity or multiformity, as a pathological change, once more, upon anatomical grounds. The method employed by him in making his investigations, his large use of fresh sections in his inquiries into fatty degeneration of the tissues, render his views upon minute histological changes in the kidney very valuable. At page 1414, he writes: "Among the kidneys I examined which had furnished distinct amounts of albumen during life, I distinguish one class in which, to the naked eye, there are no notable pathological changes whatsoever to be remarked upon. I separate a second class of kidneys, which show blood-congestions distinctly abnormally distributed through them, although presenting no particular glandular or interstitial changes (*Stauungsniere*). Thirdly, I met with kidneys presenting marked cloudiness; and fatty changes in their renal epithelium, but without interstitial thickenings; kidneys of an acute disease-process, which justified the conception and confirm the existence of parenchymatous nephritis." We infer, however, from what he advances, that it is rare rather than common for persons to die in this stage of disease, and for kidneys to be found with changes wholly confined to the epithelium lining their tubes. The fact which he brings into prominence, and the one which our experience entirely confirms, is the impossibility of making a hard and fast distinction between parenchymatous and interstitial nephritis; for the pathological facts are all against it. Even in acute nephritis, interstitial accumulations of nuclei in the intertubular substance, in parts or patches, more or less in quantity, are invariably encountered; and, as Klebs says, these are the only renal changes which really deserve the name of nephritis. The slighter the kidney-affection, the fewer and smaller these interstitial alterations are; whereas, the severer the original inflammatory action, and the more frequently it is repeated, the more these nuclear interstitial growths increase and extend into each other, the Malpighian bodies generally presenting thickened capsules, becoming contracted into tiny round fibroid cases, their glomeruli or tufts being found in every stage of degeneration, while the blood-vessels of the organ present thickened walls and intima. (Observe, not the cause, but the consequence of chronic inflammation, is his opinion.)

Now this change, he continues, is not confined to the small red granular kidney, as has been asserted; it is found in common in the largest white and in the smallest red kidney. Hence the difference between the two is one of degree, not of essence; it is the acuteness, the extent, the amount, of the change, rather than its actual histology, which leads to the difference of aspect in the kidneys, and in the resulting phenomena. These he next proceeds to point out.

The amount of interstitial thickening and number of the glomeruli affected, the localisation or generalisation of the mischief, the rapidity or gradual nature of the change, involve secondarily the nutrition of large or small tracts of the renal epithelium, which undergo either sudden necrosis, or molecular fatty crumbling, or gradual simple atrophy. With the first two changes most observers are well acquainted, but upon the last-mentioned, simple atrophy, less has been said. In this simple atrophy, the cells are not swept away; their nuclei remain distinct, but the protoplasm of the cells wastes and disappears.

In the parts where the mischief is proceeding, the secreting structures shrink and atrophy, but islets of healthy unaffected structure intervene between them, the healthy parts are raised and of natural colour, the affected parts are pale and sunken. One remarkable feature on which he insists, is the variety of change he noticed even in prolongations of the same tubule; at one part, shrinking and atrophy of its cells; at another, dilatation and varicosity, with flattening of the cell linings; at

another, entire denudation, the bare walls only of the tubule remaining; while yet in another the tube is wholly distended with conglomerate plasma, and its lumen blocked with casts of various kinds, containing detritus and white and red blood-cells. In some forms much more than in others (a class of cases he subsequently offers reasons for separating), various-sized ecchymoses are met with, both between the tubes and inside the Malpighian bodies, and are continued down the tubuli; while in other forms there is much more oedema into the intertubular spaces.

For the most part, then, he views the changes in the epithelium in chronic Bright's disease not as primary, but as secondary to interstitial changes, which have modified the circulation through the glomerules, or interfered with the normal nutritional interchanges by formation of barriers between the capillaries and the tubes with their epithelial linings; and, far more frequently, the changes in the epithelium are those of atrophy rather than of active proliferation, although nuclear growths are found in parts extending into the interiors of the tubes. Tubules filled with fatty contents, he writes (page 1,434), belong to the most exceptional appearances; even in his mottled kidney, either he found the entire diameter of a tortuous tube in the cortical portion reduced to the breadth of one or two cells only, or the tubule dilated and filled with clear fluid, its epithelium not swept away, but flattened out or levelled lower; or, thirdly, the individual cell-territories in the tubuli were broken up and indistinguishable, and small round white cells or free nuclei, some fatty, some finely granular, were substituted for them.

That a close relation must exist between the changes in the tubes and the separation of these from their capillary blood-supplies, and that the nutrition of the renal epithelium must be impaired by whatever interferes with the blood-supply to the organ, whether occurring, as in eclampsia, sometimes by spasm of the afferent arteries, or by swelling and thickening of the epithelium in the glomerules, or dropsical effusion, or interstitial nuclear new growth between tubules and capillaries, who shall dare gainsay? But as to the primary feature of the change, and the secondary consequences, and why, in one and the same kidney, we should encounter tubules, some shrunken, some dilated, some fatty, some with their cells merely atrophied, we are left a good deal in doubt by Weigert; and each one of us, perhaps, could fill up the picture after his own special bent, theory, or imagination. Weigert inclines manifestly to the belief, although he does not urge it as an article of cardinal faith, that the interstitial change is due always to some primary irritation (*reiz*); and that the tubal changes are always secondary, although the small red granular kidney was not, as Dr. Johnson believed, produced by the collapsing of the walls of the tubes, denuded by desquamation of their linings.

He does not think that the renal cells die strangled because compressed by the interstitial growth, but because they are starved; and he finally arrives at what we may accept as a general pathological axiom, which certainly holds true for the kidney: that, given insufficient blood-supply for the requirements of the organ or gland, the glandular epithelium suffers much in its nutrition, atrophies, or perhaps necroses long before the connective tissue suffers at all.

If you would see how much there is in common to the pathological processes which formed the large white contracting and the small red granular kidney, you must compare chronic, *i.e.*, long-standing, cases together, not chronic changes with those which are evidently of quite recent date. The truth is that, in renal disease, if we exclude what are obviously quite acute changes, there is no such histological or pathological difference as justifies the separation of the small red granular kidney from the large mottled, and in parts contracting, organ; and the advocates for strict dualism overlook the midway forms, the large red kidneys and the small granular white ones.

Weigert discusses the reasons of the difference in colour between the red and the white kidney. The whiteness of the kidney is due to its anæmia, its yellowness and opacity in parts to fatty degeneration. Interstitial oedema or the effusion of fluid, all of which is not inflammatory, and part of which in a dropsical person may be reasonably thought dropsical, is, he thinks, the real cause of the anæmia and swelling of the cortex in the large white kidney.

In health, no doubt the capsule of the kidney plays no unimportant part in furthering the flow of urine by resisting the blood-pressure; if the capsule be tight and unyielding, and blood be flushed through the tufts, its circulation through the organ will be quickened by the resistance of the capsule; conversely, if the organ be dropsical, its tissue macerated by effusion of blood-plasma (and the intertubular spaces in the cortical portion especially admit of such anasarca), the fibrous capsule will offer less resistance to the expanding force of the blood pumped into the kidney, and exhibit less elastic resiliency. Now, the cortical portion of the kidney is that part always which presents most

œdema; first, because by original construction the trabecular network of the gland is least developed in this situation, and because some lacunar interspaces exist here between capillaries and the tubes. Inflammatory changes of the capillaries lead to the transudation of blood-plasma in this situation most readily; and, in point of fact, in recent acute nephritis, a wide separation of the tubules from the capillaries is most apparent. The capillaries are further remarkably empty. This cannot be, however, as Dr. Johnson taught, because the tubes were swollen and compressed them; since, in that case, we ought to find the epithelium lining them in a state of active proliferation, which is certainly for the most part not so.

Interstitial œdema then precedes anæmia, and it also aids in its determination, both by rendering the capsule more lax, and by separating the blood-cells further from the renal epithelium; and just as it makes the skin white, so will it make the kidney, by relatively increasing its bulk, and separating its capillary meshworks more widely than normal.

The most sudden cases of arrested circulation, or blood-stasis, such as occur in cholera, septic poisoning, poisoning by phosphorus and chromate of potash, act by stopping the passage of the red blood-cells, cutting off the supply of oxygen which is essential for the nutrition of the renal cells, and lead thus very rapidly to their fatty degeneration. Here there need be little œdema, and yet sometimes there is much pallor of the cortex from anæmia and accumulation of fat in the tubes. A kidney may be very fatty, it is true, and yet not look anæmic when its venous radicles are highly blood-charged, as in the kidney secondary to heart-disease, which presents a purple or grey-slate colour.

The greatest amount of œdema of the organ is found in the white mottled kidney of about three or four months' duration, when time enough has elapsed for the establishment of some hypertrophy of the heart and the kidney is both very anæmic and fattily degenerated in its cortical portion, and the circulation is by œdema and interstitial hyperplasia most of all impeded. When the hypertrophy of the heart compensates the circulatory obstacle more, the circulation through the least diseased parts becomes easier, and a great contrast is presented between the red and the white parts, which gives the organ its mottled aspect.

The more insidious in its commencement the interstitial disease is, and the more gradual it is in its course, the more time is afforded for cardiac hypertrophy to take place, which compensates for the blood-defect, and overcomes the anæmia, and explains the greater redness of the small granular atrophic forms; further, in these slowly forming atrophic forms, we encounter usually least fatty changes in the renal cells, because the nutrition of these is gradually, not suddenly, interfered with. Still, every now and then, we find that these small red granular kidneys have become extremely fatty, perhaps rapidly so, when the heart's force has suddenly failed through overwork, secondary degeneration, or myocarditis. Local conditions, arterial territories specially blocked, must be held to explain why some parts become far more fatty than others.

While recognising that there is much pathologically in common to the large white and the small red kidney, Weigert admits (page 1452) that it is hardly likely that the one ever becomes the other. The large white kidney certainly suffers contraction, if life be maintained long enough; but the excessive anæmia and fattiness of the white and mottled kidneys are grave difficulties to set against such a re-establishment of the circulation as is obvious in the extreme red atrophy.

Weigert's subgrouping of Bright's disease is as follows.

FIRST GROUP, ACUTE NEPHRITIS.—*Anatomical features:* Small cellular interstitial growths; some small scattered hæmorrhages. *Clinical phenomena:* Scanty urine, with abundant albumen and white and red blood-cells in it; casts, generally œdema; no hypertrophy of the heart.

SECOND GROUP, SUBCHRONIC OR CHRONIC HÆMORRHAGIC NEPHRITIS.—*Anatomical features:* Much interstitial increase of connective tissue thickened, and contracted Malpighian capsules; endarteritis obliterans; no contraction of the entire kidney.

THIRD GROUP, MORE CHRONIC NEPHRITIS.—Noticeable naked-eye granular contraction of portions of the organ, besides other larger portions of the kidney in which healthy parenchyma is preserved. *Clinical phenomena:* Hypertrophy of the heart; varying amounts of anasarca and of albumen in the urine, according to the amount of urinary water excreted.

FOURTH GROUP, MOST CHRONIC NEPHRITIS: GRANULAR ATROPHY.—*Anatomical features:* Kidney much contracted; very little parenchyma maintained in integrity; the granular interstitial growths have extended into each other. *Clinical features:* Abundant urine; scanty albumen; no anasarca; considerable hypertrophy of the heart.

The first three groups comprehend mixed red and white mottled kidneys, of which the first is chiefly large and red-grey; and the third,

subnormal in size, and rather grey-red in colour. The fourth group presents much atrophied kidneys of non-uniform colour, red or grey. Amyloid complications chiefly affect groups two and three.

Weigert has perhaps insisted more strongly than any writer on Bright's disease in the last twenty years, upon the points common to the various forms of chronic renal degeneration; and, while admitting, what all must, the gross distinctions between interstitial and glandular, intertubal and intratubal increase of material, and difference in the renal aspect and in the clinical symptoms thus brought about, he compels us to revert somewhat to the original views of Bright, Reinhardt, and Frerichs, and accept the fact that interstitial new growth—now more rapidly, now more gradually progressing—is the fundamental pathological principle of the whole disease; and this is essentially inflammatory in nature.

He proves to demonstration that the old conception of Bright's disease was not wrong, which explained it as one uniform inflammatory change, prolonged through various stages, complicated by secondary compensative hypertrophies, both in the sounder parts of the organ itself and in the heart, and produced by nature in her effort to repair the damage done.

He does not say that the one form becomes the other, but that there are midway forms between the large white and the red atrophied kidney, with anatomical features in common to both; mid-forms not, perhaps, presenting quite so much fatty necrosis of the epithelium in the tubes as marks some types of the large white kidney; but presenting much more acute inflammatory changes in the tubes than those which attend the most typical forms of the small red kidney; and the inference which he draws is quite justified by the facts, that the distinction between them is one of degree, not of kind, and that, when you come to draw a definite line, it becomes impossible to say where to fix it.

Cohnheim's views (*Vorlesungen über Allgemeine Pathol.*, 2 Abtheil. Harn-Apparat, page 273, 1880), are essentially those of Weigert; but he makes its first beginnings and the points of departure between the varieties easier of apprehension.

He says: Glomerulo-nephritis, or disease which first shows itself in alterations of the Malpighian bodies, is acute Bright's disease; whether the alteration that takes place in the tufts and capsules, and their endothelium, be sudden and extensive, or gradual and circumscribed, makes the whole difference of the ultimate pathological changes and of the issue. The more acute cases either die or recover; those which commence more gradually progress insidiously, step by step, to more or less extensive interstitial new growth of connective tissue, and pass on towards greater or less contraction of the secretory structures. There is no need to assume that kidneys ever were once swollen, and large and white, before they became contracted, for it is not requisite that they should pass through this ordeal. Only, when you find a large kidney, you are quite justified in saying, here is a mischief of moderately recent date; whereas, when presented with a small contracted red one, it is, in our present experience, impossible to say when the disease first began—only that it must date back some long period.

He tells us what the changes are which he has observed, confirming Klebs's observations of the swelling up of the epithelial layers over the tufts in the glomeruli, and the filling up of the free space between the tuft and the capsular walls with nuclear growths, perhaps of multiplying connective-tissue cells. A healthy condition of the epithelium prevents the transudation of albumen through the capillary walls of the tuft; an unhealthy swollen or thinned condition of the epithelium and the walls of the capillaries leads to transudation of blood-plasma in this situation, and to albuminuria. Further: such changes in the tuft lead to embarrassment of circulation through the organ, slackening of the blood-current, and diminution of the blood-pressure through it.

Experiments on animals by tying renal arteries, experiments by disease on man, as in cholera, epilepsy, eclampsia parturientium, tetanus, when spasm of small arteries may lead to complete ischaemia in these organs and total temporary arrest of circulation through the kidneys, illustrate the processes of disease, and make it comprehensible.

Diminution in the supply of oxygenated blood leads to stasis in the intertubular capillaries, to migration of white and red cells into the intertubular spaces.

The more on one side the *reiz* or source of irritation affects the glomerular tuft, the more general and extensive is the retardation of the circulation through the organ; and starvation-changes in the blood, degeneration of the tubes and of the renal cells, œdema and anæmia of the kidney, mark the process; whereas, the less the glomeruli are affected, or the greater the number of them that offer no obstacle to the blood-passage, the more general hyperæmia will prevail.

For acute changes—scarlatinal nephritis, nephritis after diphtheria, septicæmic nephritis—we can accept his explanation as all-sufficient; these cases fall into the hands of the pathologists, and the facts have been repeat-

edly confirmed. It has remained for Cohnheim and Weigert to extend the picture, to plead the probabilities in favour of the nephritis of insidious origin still commencing in much the same way. Some irritant in the blood circulating through the tufts stirs up the strife; as we can notice its acting suddenly and acutely, so we can imagine its non-continuous or intermittent action, according as particular irritants accumulate in the blood; or, although only slightly at any one time, persistently and progressively increasing as the blood deteriorates in quality. We find illustrations of the persistent blood-irritants damaging and inflaming capillaries, in gout, syphilis, malaria, in poisons which act remittingly, in lead, alcohol, and in the effects of burns and local inflammation of the skin; products of tissue-metamorphosis, suddenly thrown into the circulation, either blocking the glomerular tufts or inflaming them.

Stagnation of the blood-current, and impurity or special impropriety of the blood, induce the epithelial and interstitial changes which progress, unequally certainly in different forms of disease, but *pari passu*, and together constitute Bright's disease. As the contents of the tubes waste, so these atrophy and contract, and their room is filled up and even overfilled by interstitial increase or growth. Then the elevated parts of the kidney become imperfectly vascular, anæmic, and grey, and represent the parts in which interstitial tissue-growth has overwhelmed secretory structures and capillaries; while the sunken parts are red, and represent capillary net-works permeating atrophied and shrunken tubes.

That the walls of the arteries generally throughout the organ should be thickened in this granular contracted kidney, is not singular; it is not the cause of the change, but the consequence of it; and this Cohnheim infers from its invariability in every other organ which is the seat of chronic inflammation—in the liver in chronic hepatitis, and in chronic pneumonia.

This question, however, of the changes undergone by the arteries, and the hypertrophy of the heart, it is my intention to reserve to my last lecture.

Let me now sum up my case. It has been my endeavour to put before you a critical review of the opinions that have been brought forward of late years upon the subject of Bright's disease. What is it? What constitutes it pathologically? What are its symptoms? What separate varieties are there of it? Were ever questions more vexed? Bright, it is well known, recognised three typical forms of diseased kidney; and at the last thought that they might all be successive stages of one and the same process of disease. How near his views were to those which are now obtaining general assent is at least extremely interesting.

My friend Dr. Quain called my attention recently to an episode which I deem well worth making public. It was at an early meeting of the Pathological Society that he brought into the room these two pictures of a large white and a small granular kidney, and submitted them to Dr. Bright's inspection. "Now, Dr. Bright," said he, "which of these kidneys do you say belongs to your disease?" Bright answered: "I should claim them both."

It is now pretty generally allowed that the hyperæmic kidney, the large red grey kidney of acute parenchymatous nephritis, becomes the large white anæmic and fatty organ; and further, that this swollen, and at first smooth-surfaced, kidney does become mottled on section, uneven and coarsely granular upon its surface, and that it toughens, in part contracts, and in part atrophies and becomes smaller (although there is little agreement of authorities upon its ever coming in any way to resemble the atrophic finely granular small red kidney). Further, the tissue-changes by which this form of white granular kidney is brought about are confessedly inflammatory from first to last. This small red granular kidney, however, is by a large majority of trustworthy guides—Dr. Johnson, Traube, G. Stewart, Gull and Sutton, Kelsch, Bartels, Charcot, Rendu—held to be a distinct form of disease. Why? Mainly because the tissue-changes by which it is surmised to have been brought about are presumed to have been non-inflammatory. The cause of the change is pleaded to have been, from first to last, an interstitial or matrix tissue overgrowth, strangling the Malpighian bodies and blood-vessels, starving the renal cells, and inducing an atrophy of the secreting tubules.

The whole conception of cirrhosis, interstitial overgrowth, is founded upon the hobnail liver; and that notion of strangling of secreting structures and blood-vessels is a fundamental error. It is an allegory, a figure of speech, by which some of the facts of pathology are rendered more easy of comprehension to minds that are wholly untutored. But it is well nigh time that it should be swept away.

Carl Weigert, Cohnheim, Rosenstein, Bamberger, Greenfield (*Pathological Transactions*, 1880, vol. xxxi, p. 157), Saundby (*ibid.*, p. 148), are of opinion "that the small red and large white kidney, and all the intermediate varieties, are the result of an inflammatory process, affect-

ing all the tissues of the organ (not one to the exclusion of all the rest), but varying very greatly in its intensity".

The parenchyma, or the glandular secreting structure, as the most organised tissue, suffers most in proportion to the acuteness of the inflammation. So far from the large pale kidney in its contracting, *i.e.*, more chronic, form, being separable from the red atrophic kidney, because the inflammatory changes are limited to the renal cells and to the tubules, the fact is absolutely untenable; so obviously untrue is it. This large white kidney is the form in which, as Dr. Greenfield has shown, the tubular changes are attended by the most self-evident interstitial nuclear overgrowth, and in it the most obvious change is circumtubular, or intertubular, or circumglomerular; whereas, in the small red atrophic kidney, except close to the capsule, which is thickened, there is no such considerable interstitial overgrowth. The capillary walls, the arterial walls, the walls of the tubules, are thickened; but the tubules are collapsed, chiefly by atrophy of their renal cells. Thus a distinction between the two forms, if we admit the commencement of both by changes in the glomeruli mainly interfering with the circulation through these organs, cannot be maintained upon strict pathological grounds, although it is readily conceded that one form is more distinctly inflammatory, the other more subinflammatory; that in the one, multiplication of degenerate cells or degradation of the tissues takes place both in and outside the tubules; while, in the other, the changes are mainly atrophic so far as the tubules and their lining cells are concerned. Finally, we must admit that the indefinite number of intermediate forms (asked for by Dr. Wilks in former times) between the two typical varieties are now admitted to exist in great number, and become an ever stronger argument in favour of the doctrine of one Bright's disease.

As to the beginning of both forms, the pathologists trace the commencement of the large white kidney up to the glomeruli, saying that the epithelioid lining swells up, its nuclei multiply, squeeze up the capillary tufts, and stop the blood-supplies; and tell us that the small red granular kidney begins by an interstitial new growth both inside and outside the Malpighian bodies, gradually interfering with the blood-current through the tufts, and only obviated from starving the organ altogether by the time given for the establishment of short circuits by collateral channels.

The issue in each individual case, then, appears to turn upon the following things 1. Upon whether the circulation through the organ is suddenly checked, or very gradually altered in its direction. 2. Upon whether the matrix tissue and the intertubular spaces are or are not soddened by dropsical effusion. 3. Upon whether the capsule of the organ is gradually thickened by subinflammatory fibrous growth, and resists the blood-pressure or yields to it—a factor of no small importance towards the quickening or slackening of the blood-current through the organ. 4. Upon the amount of blood-circulation still feasible through the glomeruli: enough to maintain the renal cells at a low rate of function; enough to secure parenchymatous or glandulous swelling; enough to provide for some inflammatory exudation or the development between the tubes and capillaries of a low embryonal form of nuclear tissue. 5. Upon the maintenance or failure of the blood-pressure, upon the transudation or not of urinary water, and so upon the blocking up or maintained patency of the lower excretory system of urine tubes. 6. Upon the establishment or not of a collateral blood-circuit, the vasa afferentia passing directly into vasa efferentia without going through a first capillarisation; the lowest tiers of Malpighian tufts becoming, or not, greatly hypertrophied; the sluices of the vasa recta by direct arterial conduits becoming employed. 7. Upon the general health of the individual, and the capacity of his heart to become hypertrophied.

In my next lecture, I propose to discuss matters which have been the subject of much controversy: the alterations of the arteries, and the hypertrophy of the heart; and to submit to my hearers some facts about Bright's disease of my own compilation, the outcome of my hospital experience.

CINCHONA IN JAMAICA.—From a memorandum of Mr. D. Morris, Director of public Gardens and Plantations in Jamaica (dated January 31st, 1881), it appears that, in the hurricane of August 18th last, many thousands of cinchona trees were blown down and uprooted. In consequence, it was necessary to resume barking operations in spite of the unfavourableness of the season. The bark was cured with such success that the whole consignment, consisting of 180 bales, and weighing in the aggregate 14,397 lbs., was ready for shipment within a few weeks of the occurrence of the hurricane. The total results of the cinchona sales during the last fifteen months now show a gross return of 41,696 pounds of dried bark as having been shipped, yielding a total value of £8,167 10s. 8d.