THE LUMLEIAN LECTURES ON BRIGHT'S DISEASE.

Delivered before the College of Physicians.

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LECTURE II.—PART I.

IN 1863, Rosenstein's work on Kidney-Disease was issued from Berlin. Like Frerichs, he regarded Bright's disease as one essentially uniform pathological process, encountered in various stages, according as life was cut short or prolonged; the kidney at the time of death presenting different aspects, according to the stage reached, and the particular tissue at that time predominantly altered. But his synonym for it was "diffuse nephritis", by which he implied that every element in the kidney—tubes, blood-vessels, and matrix-tissue—were involved.

He separated various renal affections, in which albumen occurred in the urine, from Bright's disease: 1. The congested kidney of passive hyperæmia; 2. The slighter catarrhal forms of nephritis, in which albuminuria was often a very temporary affair; and 3. Amyloid degeneration.* His conception and his description of the mode of commencement of diffuse nephritis, however, entirely corresponded with those changes in the renal epithelium, to which Virchow had assigned the name of parenchymatous inflammation. He says: The renal cells and the matrix-wall of the tubes swelled up simultaneously in the first stage of hyperæmia; in the second stage, exudation took place, not on the bare surface, but into the renal cells themselves, which distended the tubuli and encroached upon the intertubular spaces, and squeezed the blood out of the cortical capillaries. Two courses were now open (the third stage); either the epithelium might decay, the secreting tubes atrophy and spontaneously collapse (as Dr. Johnson had surmised); or the inflammatory changes might extend to the interstitial matrix-tissue of the glands, which became, either locally or generally, the scene of cellular hyperplasia.

There is a good deal here, of course, taken at second hand from the pathological authorities of the time; and there is no particular advance, except in interpretation of the facts observed, upon Frerich's ideas; but the description of the symptoms was, and is still, admirable; and the book continues to be in Germany the best text-book of renal diseases.

In 1860-61, Dr. Dickinson published two papers in the *Medico-Chirurgical Transactions*, vol. 43, page 144, based upon clinical records and necropsies at St. George's Hospital. He divided Bright's disease into two varieties: 1. The tubular disease, primarily a catarrhal affection of the renal tubes, leading to the large, smooth, white, or mottled kidney; and, in cases which lived long enough, advanced to some degree of atrophy. 2. The intertubular disease, in which he surmised that an exudation, thrown out between the tubes, finally starved and involved both secretory tubes and Malpighian bodies in gradual destruction—this process leading ultimately to the formation of the atrophied granular kidney.

Dr. William Roberts, in his *Practical Treatise on Renal Disease*, published in 1865, treats the subject, as he writes (page 296), "rather from a clinical than an anatomical point of view". A good many new anatomical features in the kidney were just then being brought to light by Henle and Schweigger-Seidel. He classified Bright's disease under two main heads, as acute or chronic. The former corresponded to the inflammatory dropsy of the old physicians; the desquamative nephritis of Johnson; the first stage of Frerichs; the parenchymatous nephritis of Virchow; the acute diffuse nephritis of Rosenstein; and the acute tubular disease of Dickinson. The chronic Bright's disease was a less satisfactory group, involving, as it did, relapsed or protracted acute cases, and others which had been chronic from the beginning. He pronounces himself promptly on the subject of fat in the renal substance, and in the epithelium of the tubes, as an alteration associated with most varied pathological changes, and special to no one type of renal degeneration (page 297). He recognises three types of chronic Bright's disease: 1. Large white kidneys, lapsed acute cases; 2. Cases chronic from the beginning, red granular contracting kidney; 3. Lardaceous or amyloid kidneys.

* Rosenstein also separates the fat kidney, like the fatty liver, wholly from Bright's disease, and from amyloid degeneration. This is the kidney which Rokitansky described as "steatosis". I am by no means clear what kidney is here intended. One case after poisoning by phosphorus is included in this chapter.

The first edition of Dr. Grainger Stewart's *Practical Treatise on Bright's Disease* was published in 1868. He makes catarrhal and croupous nephritis the first stage of parenchymatous nephritis, but the main feature of his work is the accurate distinction drawn by him between that secondary atrophy with coarse granulation, which follows in some protracted subacute forms of tubal or parenchymatous nephritis in which the renal epithelium has been destroyed and faintly degenerated, and the interstitial tissue only relatively increased, and the primary insidious cirrhotic atrophy of the kidney, in which the interstitial tissue is absolutely increased in quantity by active hyperplasia. He, too, is the earliest writer to state how many mixed forms of renal degeneration are encountered in practice; as, for example, of cirrhosis with parenchymatous inflammation, and of parenchymatous inflammation with superadded amyloid degeneration.

Bright's disease was shrinking within narrow bounds. First, it had been held to comprehend every renal affection in which the urine was albuminous; then it could be applied as a synonym to any kind of nephritis; but, in 1869, the Nomenclature Committee of our College determined to separate acute Bright's disease from chronic morbus Brightii. Acute Bright's disease was to be a name applicable to acute renal dropsy, as this presented itself after scarlatina or exposure to cold. Chronic morbus Brightii was to serve as a group, having three subdivisions: (a) granular; (b) fatty; (c) lardaceous kidney.

In 1870, Professor Klebs of Prague (*vide Handbuch der Pathol. Anatom.*, Band I, s. 645) found minute anatomical reasons for separating altogether that acute form of nephritis which followed scarlet fever, diphtheria, small-pox, and other acute febrile disorders, from acute Bright's disease, acute diffuse nephritis as described by Virchow and Rosenstein.

In the postscarlatinal disease, he, with Professor Axel Key, had discovered that the brunt of the disease did not fall in the first instance upon the renal epithelium and the tubules, but upon the glomeruli themselves. The Malpighian capsules were constructed externally of a filamentous framework of fine fibrous tissue, wholly distinct from a cubical pavement-epithelium lining their interior; elongated processes from the connective tissue framework of stellate form, and distinguished by angular nuclei, served, in the healthy state of the parts, to restrain or limit the movements of the several claws or loops of the capillary lobulations inside the glomerules. But, in the form of disease under notice, these connective-tissue corpuscles swelled up, the nuclei multiplied in their interiors, until the whole glomerule, swollen to twice its natural size, consisted wholly of closely packed nuclei; which either compressed, emptied, or obliterated the capillary tuft.

It was thus that the blood in the intertubular capillaries was brought to stand still, for none passed through the glomerule; hence the general capillary turgescence, hyperæmia, with the distortion, pallor, and undue prominence, of the glomerules, which many other observers had noticed; and hence, too, most of the subsequent events.

Facts so self-evident could only have been overlooked, because the opportunities for investigating them had been few, for few cases of scarlet fever died just at this stage of the disease; and because, at a later stage, the swelling up of the tubes rendered the primary change more difficult of recognition.

It is the opinion, however, of later writers, that the original facts, as interpreted by Klebs and Key, have been amply confirmed, and that this is the original lesion. In the kidneys of those who die in a sufficiently early stage of scarlatinal nephritis, little else than this swollen nucleated condition of the glomeruli is apparent, the changes in the tubules or the stroma of the organ being quite unimportant. The tissues round about, as often described, are hyperæmic, just as in embolism, from blood-stasis, or greyish-red, as the epithelium in the renal tubes a little later on swells up, the vascular zone and tufts of vasa recta in the cortico-medullary part being intensely blood-gorged.

Let us recapitulate the events, since to some who hear me they may be novel. The circulation of the blood through the glomerules—some or all (seldom all), but yet much more universally than in ordinary nephritis—is greatly impeded, if not wholly obstructed, by the multiplication of nuclei and accumulation of albuminoid materials inside the glomerules; hence blood-stasis and hyperæmia in the intertubular capillaries, in the first place; and, later on, the patient living long enough, migration of blood-cells into the spaces between the tubes, perhaps into the tubules themselves.

Kelsch, writing subsequently in 1874, entirely confirms Klebs's view, that the glomeruli are the parts first affected; he speaks, too, of the wide separation from each other of the renal tubuli by an embryonal cell-tissue; refers the cloudy swelling of the renal epithelium and subsequent tubal changes to blood-starvation, arrest of the normal changes, and, foremost, to the lack of the urine-water derived from the glomeruli, which ought to wash the solid renal secretion out of the renal cells.

Certain it is that, in an early stage, these cells do present a yellow coloration, refract light highly, and fail to be affected by æther; showing that the change is not due to fine fat-granules.

Klebs's discovery has become the subject of much subsequent inquiry. It has lately received the fullest confirmation at the hands of Alfred Meyer of New York (*75 Band der Sitzb. der k. Akad. der Wissensch.*, III Abth., Jänner Heft. Jahr., 1877); and by Cohnheim in his *Vorlesungen über Allgemeine Pathologie*, 1880.

In 1874, M. Kelsch published in Paris his views on Bright's disease, in which he protests with some bitterness against the German conception of its being a morbid process divisible into three stages, like a play in three acts. He thinks the first stage is evolved entirely out of the imagination of the pathologist; that the second—Virchow's parenchymatous inflammation—has nothing really in common with inflammation; that the changes in the cells should be regarded as anæmic necrosis. He separates the congested kidney, with its morbid interstitial changes, from nephritis Brightica; considers—as, indeed, Klebs, Cohnheim, and most recent writers do—postscarlatinal nephritis as involving true interstitial changes, as commencing by what he calls the deposition of embryonal cells, multiplication of nuclear cell-tissue around and in the glomeruli; regards the changes of the renal epithelium as wholly secondary, or as retrograde metamorphoses, the consequence of an impeded supply of nutritive fluid. The period of embryonal tissue-growth, according to him, is marked by general swelling of the organ, but terminates by fibrillation of the connective tissue and atrophy. Bright's disease, for him, is interstitial nephritis. And descriptions of the process show his indebtedness to Lecorché for his account of *schérose rénale*, and to Grainger Stewart for his of kidney-sclerosis.

Kelsch, then, admits differences of issue, but recognises much uniformity in the actual pathological changes, in which he is in accord with the best latest observers. His work was followed in France, in 1874, by the appearance of M. Charcot's *Leçons sur les Maladies du Foie et des Reins*. Charcot is a much more decided separatist or dualist in his views on Bright's disease, being quite of the same idea as Grainger Stewart, Johnson, Dickinson, and Bartels, that the small red granular kidney owns a pathology wholly apart from the white kidney, even in its ultimate contracted state.

In 1875, two memorable works appeared, which have advanced our knowledge of renal disease considerably. Lancereaux's article "Reins" was published in the *Dictionnaire Encyclopédique des Sciences Médicales*. In this, the morbid anatomy of Bright's disease and its varieties is minutely described; and the controverted points, as to the why and how the peculiar circulatory arrangement and anatomical disposition of the tubes compel certain consequences, are ably pointed out. Besides this, Professor Bartels's "Krankheiten der Harn-Apparates" came out in Ziemssen's *Handbuch*.

The merit, as we think, of Bartels's last great work attaches most of all to the clinical observations contained in it. Upon minute pathological points, other writers, possessed of more practical knowledge of histology, may be more trusted. Upon gross differences, he was as competent to pronounce an opinion as any one was; and the distinction which he draws between the various types of diffuse renal disease must be admitted: they claim universal approval. In his work, he describes:

1. The hyperæmic changes of the kidney, active and passive.
2. The ischæmic or blood-stasis changes, of which the choleraic kidney is taken as an example.
3. Parenchymatous inflammation, of which he makes two subdivisions: (a) the acute, which may become chronic; (b) the insidiously commencing, or chronic from its outset. Most physicians will admit the accuracy of the distinction made here, and its practical importance.
4. Interstitial connective induration-changes, or renal cirrhosis. As to the mode of commencement of this type, Bartels is far more guarded and silent than Kelsch was, or than most authors who had preceded him, and incurs no risk of the imputation of having evolved any pathological problem out of his imagination. He discards Gull and Sutton's hypothesis, but offers none of his own.
5. Amyloid degeneration. The general symptoms of renal disease, the importance of ascertaining the functional capacity of the kidneys, towards distinguishing one variety of renal degeneration from another, are pointed out by the hand of a master of clinical medicine; and we venture to predict that his chapter on uræmia will long be referred to as the best on that subject that has been compiled in any European language.

The history of Bright's disease has been brought down by us to 1875, the date of the appearance of Professor Bartels's article in Ziemssen's *Cyclopædia*, vol. ix; but it would be left very incomplete if we left it there, and did not review Professor Bamberger's very remarkable article

on Bright's Disease and its Relation to other Diseases. This appeared in Volkmann's *Sammlung Klinischer Vorträge* in 1879 (No. 173, p. 1533). Bamberger commences by distinguishing between the large white, the contracting white, and the small red granular kidney. He states that it was found essential for statistical purposes at Vienna to distinguish between them, and make three subdivisions of morbus Brightii—the acute form, the chronic form, the renal atrophy form: separations which closely correspond with Frerichs' three stages of the disease, although by no means implying that the ultimate small red granular kidney was, at any stage of its history, a large smooth white organ. He fully admits the difficulty occasionally presented of placing the kidney-case at the necropsy into the category to which it strictly belongs; entirely corroborating what Virchow said in his *Cellular Pathology* (iv Auflage, p. 447), that we encounter kidneys after death in which parenchymatous, interstitial, and amyloid changes are so intermixed, that it is impossible to say what condition of tissues prevails.

Aufrecht's experiments in tying the ureters of animals proved that both parenchymatous and interstitial nephritis might be provoked by one and the same cause—obstructed urinary outflow; temporary obstruction producing parenchymatous changes; more prolonged pressure upon the tubules, hyperplasia of connective tissue. (*Centralblatt für die Med. Wissenschaften*, 1878, No. 35.)

But Bamberger's own personal experience, the microscopical examination of every large white kidney that came under his own observation during a whole year, taught him that, in every instance, interstitial hyperplasia was an adjunct of the parenchymatous swelling of the tubules. The increase of connective tissue, it is true, was not equally diffused all through the organ (as in extreme red atrophy), but localised here and there in little nest-like patches, where obviously the interstitial or intertubular spaces were widened, the fibres thickened, and the nuclei multiplied. Portions, too, of the new tissue presented fine granular fatty dottings and degeneration. Bamberger, therefore, could not go so far as the English writers, Bartels, or von Buhl, and separate the large white from the small red kidney by its minute anatomy, any more than he felt justified in separating it by its etiology; and he assumes that Klebs's views, as already stated, were correct, and that glomerular interstitial hyperplasia was probably the starting-point of the changes which culminated in parenchymatous degeneration.

Clinical observation again led him to the same conclusion; namely, that, although two distinct types of disease might exist, mixed forms were to be met with; and that in every grade of intermixture, and complicated occasionally with amyloid degeneration as well. In practice, he had encountered cases where every symptom during life, insidiousness of origin, frequent micturition, etc., suggested granular atrophy, yet which the *post mortem* examination showed to have been produced by ordinary (chronic) parenchymatous change; and others presumptively parenchymatous from history and course, which lived a very long time, and finally exhibited very much contracted kidneys. Clinical histories, therefore, although great helps, could not be entirely relied upon for distinguishing the one from the other. If it were asked on what features we rely most to guide us to a correct diagnosis during life, most clinical physicians would answer, "The duration of the case, the early or late appearance of dropsy or of blood in the urine, whether hypertrophy of the heart co-existed or not". Yet none of these symptoms, singly or together, can always be trusted to.

Bamberger holds that the question of unity or dualism in Bright's disease is an open one, and that the small red granular kidney may still turn out to be what Bright and Frerichs thought it to be—the final stage of a process essentially and pathologically the same as that which leads to the formation of tubular or parenchymatous disease. But, pending decision, he found it advisable to divide his cases of Bright's disease into the following broad categories: 1. Those in which the kidney-disease is primary, original, self-initiated (*selfändige*); of these he had collected 807 cases, or 33 per cent. of his grand total; 2. Those in which the kidney-disease admits of having been secondary, because associated in the same body with a number of other profound and important changes—changes which might be pleaded as sufficient causes of the renal degeneration, impossible to be regarded as consequences of it, and not to be looked upon as accidental complications. The total number of these secondary renal cases which he brings forward is, inclusive of 120 doubtful ones, 1,623, or 67 per cent. of his grand total. He explains by a happy figure how these classes differ one from the other, not so much in feature or in anatomical fact as in interpretation and prognosis, by saying, "Look at pneumonia as an acute idiopathic phenomenon, and pneumonia incident to rheumatism, to septicæmia, to fever, to the puerperal state".

The primary renal disease is more typical, the secondary renal disease less uniform. In 42.6 per cent. of the primary renal cases, the heart is found to have undergone hypertrophy; whereas in the secondary

cases, excluding, of course, those secondary to valvular lesions, endoarteritis, and emphysema, the heart is only implicated to the amount of 3.3 per cent. of the cases.

The secondary forms may be very obvious or very insidious, acute or chronic; at one time more interstitial, at another more parenchymatous; often mixed with amyloid degeneration; but, as a rule, the renal mischief only plays second fiddle, and is an adjunct to other serious diseases. Still, at times and in some cases, the renal clinical symptoms, although secondary, assume a great importance, and engage more attention than the general condition out of which they arise.

Bamberger's primary form of Bright's disease comprised both glandular or parenchymatous and interstitial nephritis—807 cases in all. Of these, he observed 67 cases which were acute in their commencement and course, 357 which were entirely chronic, and 383 which lived on to renal atrophy. As regards age, he proffers a most reliable table. Excluding the scarlatinal form, which, early as well as latest authorities acknowledge, is not morbus Brightii in Bright's sense, the facts stand thus.

Decennium.	Cases.	Males.	Females.
1	1	0	1
2	50	33	17
3	121	64	53
4	149	93	56
5	156	94	62
6	152	78	74
7	115	57	58
8	55	22	33
9	8	4	4

The greatest proportion of acute to chronic cases—54 to 13—occurred between the ages of 20 to 40; between 40 and 60 years of age, the chronic cases preponderated, the ratio being 214 chronic to 143 acute; while between 50 and 70 years, the large proportion of cases were atrophic kidneys. His table of the general primary diseases, to which morbus Brightii was secondary, gives us these etiological moments in the order of their frequency and importance.

Morbus Brightii.

Primary Disease.	Acute.	Chronic.	Atrophic.	Totals.	Percentages on 2,430 cases.
Tubercle; phthisis; scrofula	47	257	77	381	15.7
Valvular heart-lesions	19	117	86	222	9.1
Gravidity and puerperal state	80	56	16	152	6.3
Disorders of urinary channels	11	72	51	134	5.5
Suppurations	42	77	10	129	5.2
Alcoholism; cirrhosis	16	68	33	117	4.8
Carcinoma	13	55	35	103	4.2
Pulmon. emphysema	6	51	28	84	3.5
Typhus and typhoid	42	14	2	58	2.4
Syphilis	4	29	16	49	2.
Scarlatina	18	—	—	18	0.7
Ague and malarious fevers	1	9	3	13	0.5

Various other maladies, he admits, may be provoking causes of secondary Bright's disease; cholera, pneumonia, diphtheria, variola, scorbutus, dysentery, acute atrophy of the liver. He proceeds to argue that, if so many predisposing causes invite these localised renal pathological processes, albeit we may allow three forms or varieties of degenerative change to them, there must be some noxious influence they exercise upon the kidney which we ought to be able to discover. Do these noxious influences admit of being grouped and reckoned? Yes. 1. We can take count of certain poisonous substances—viz., phosphorus, lead, alcohol, ague, infectious fevers, decomposing pus from extensive exposed suppurating surfaces—or contaminating principles of which we have learnt in the blood, which it is the object of the kidney to eliminate from the system, although, unfortunately, it may damage itself in the task. At least one-third of the predisposing diseases probably act thus. 2. We perceive the malinfluence upon the kidney exercised by disorder of the circulation through this organ; how valvular lesions of the heart, emphysema and cirrhosis of the lungs, curvatures of the spine, invite disease in this way. 3. Lastly, we have learnt from Aufrecht's experiments on animals, and many of nature's own experiments on man—as compression of the ureters by tumours; obstruction of the urinary outlets, as effected by urethral strictures; hypertrophy of the prostate gland, and various bladder-affections—that the kidneys as secreting glands suffer pathologically, and become the seat of secondary morbus Brightii, parenchymatous or interstitial nephritis, when the urinary passages are anywhere obstructed, and the urinary secretion has to be conducted under conditions of abnormal urine tension.

[To be continued.]

THE GULSTONIAN LECTURES ON ANÆMIA.

Delivered before the Royal College of Physicians.

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LECTURE III.—PART I.

Idiopathic Anæmia (continued)—Chlorosis: Reasons for and against its separation as a Distinct Disease—Congenital Defects (Vascular Hypoplasia, Virchow) cannot be at the root of all Cases—Its obvious Relations to Altered Conditions of Life and Work—Relations to Menstrual Irregularities—Symptoms of those of Anæmia—The Blood in Chlorosis—Effects of Treatment—Cardio-vascular Symptoms of Anæmia: Cardiac, Arterial, and Venous Murmurs—Their Mode of Production—Anæmia as a Cause of Heart-Disease (Goodhart).

MR. PRESIDENT AND GENTLEMEN,—In my last lecture, I endeavoured to show that pernicious anæmia must be considered as the outcome of a severe anæmia, whether symptomatic or idiopathic, its progressive course and frequently fatal issue being induced by changes, of which there is yet but little information either in the normal formation of the blood or in its destruction; and I propose to-day to speak, in the first place, shortly about chlorosis, which I believe to be a form of anæmia depending on similar changes, and therefore to be considered as falling under the head of idiopathic anæmia. I know that this is contrary to prevalent teaching, and perhaps may be regarded as a retrograde step, for the tendency is undoubtedly rather to analyse diseases than to effect syntheses of conditions which have a superficial resemblance. But, where the distinctions are so finely drawn and so subtle as they are in respect to chlorosis, such analytical severance is hardly justifiable, perhaps harmful, and certainly productive of confusion. There is only one certain ground for such severance, and that is the one which follows from Virchow's discovery, in some cases of chlorosis, of what appear to be congenital defects in the circulatory mechanism, to which I shall presently refer. Setting that aside, there does not appear any marked distinction between chlorosis, in its development and progress, from other forms of anæmia of idiopathic origin, save only that, in many of the latter, the progress is uninfluenced by treatment. The point of view taken by those who argue for the separation is, that chlorosis is a distinct morbid entity, of which the anæmia is but a symptom;* that it is marked by nervous derangement, and frequently by menstrual disorder, as much as by anæmia; but the same may be said with equal warrant of the forms of anæmia to which it should be allied. The anæmia itself is but a symptom, which in its turn brings other symptoms after it; and in both chlorosis and in the idiopathic anæmia of the adult, the anæmia prevails over every other symptom.

The reasons which, so far as I can gather, are advanced in favour of regarding chlorosis as a distinct disease, are these: its almost complete limitation to the female sex; its apparent dependence in some way on the menstrual function, and the changes undergone by the organism at puberty; certain nervous conditions, and certain peculiarities in the composition of the blood, and the structure of the blood-vessels. To consider each of these in turn. It is well known that the female sex is more readily influenced by anæmiating causes than the male; the blood is less rich in hæmoglobin, and its quantity is less. Any influence liable to create a demand on the blood is more likely to lead in the female to anæmia than in the male; and not only at puberty, but during pregnancy, the puerperal period, lactation, and the menopause, anæmia may arise and become profound. There is no essential difference between the anæmia produced at any of these periods. Nor is the limitation to the female sex of a condition indistinguishable from chlorosis invariable. I have at present under my care a youth, well developed and well nourished, who is the subject of an anæmia conforming in its history and characters, and I may add in its curability, to the most typical cases of chlorosis; and, from time to time, such cases of male chlorosis are recorded. More than this, in later life, the male, like the female, appears to be liable to the development of an insidious anæmia, without wasting, which in all its leading features resembles

* Moriez: *La Chlorose*. Paris: Masson. 1880.