THE LUMLEIAN LECTURES

ON
BRIGHT'S DISEASE.*Delivered before the College of Physicians.*

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LECTURE I.

HIPPOCRATES, in his *Prognostics* (21), distinguishes the dropsies originating from the flanks or loins from those which are due to disease of the liver; and although, in his description of the diseases of the kidneys, we find nothing to prove that he was acquainted with any pathological conditions other than those which are provoked by gravel, calculus, or by extensions of mischief from the bladder up into the kidney, it is obvious, from remarks found scattered through his writings, that he had not failed to observe diminished urination associated with general dropsy, beginning in the feet, and attended by obstinate diarrhoea, which failed to relieve or empty the abdomen.

In Section 7, Aphorism 66, he advises that in all diseases the urine should claim special attention, since information as to the soundness or unsoundness of the body was to be obtained by inspection of this important excretion.

In Section 7, Aphorism 34, we read: Bubbles maintained upon the top of the urine signify a disease of the reins, and likewise its long continuance; a fact which remained unimportant until the end of the last century, when it was ascertained that albuminous urine held a froth of bubbles on its surface.

In Section 4, Aphorism 70, he observes that those who have their urine troubled or unclean, after the habit of cattle, are or shall be troubled with headache.

In Sir Conrad Sprengel's *Translation of the Aphorisms*, published in 1735, p. 267, I find these noticeable remarks made upon Aphorism 77 (Section 7): "The urine generally discovers to us the state of the blood: stringy and lint-like ramenta in the urine denote a crude and undigested chyle; and the thicker they are in the urine, the more there must be likewise in the blood. This kind of urine I have lately observed in a gentleman that had ruined his body by intemperate drinking and contracting great cold. He had a great appetite to his victuals, but more to his drink."... "His stomach (was) hard, painful, and swelled, his legs likewise swelled, and his face pale and bloated." This was surely a case of renal dropsy and granular kidneys.

Aretæus the Cappadocian (Adams's edition, London, 1856, p. 342) makes some observations upon blood in the urine which, interpreted by our present knowledge, and although vague and rather spoiled by being mixed up with remarks on hæmorrhoids, show at all events that he recognised the association of pallor, sluggishness, proclivity to headache, and epileptic attacks, in some forms of urinary disease, as well as general anasarca and dropsy in others. It is probable that Aretæus was a contemporary of Galen, which takes us back, therefore, to the certain date, A.D. 131.

Towards the close of the sixteenth century, necropsies became more frequent; and several medical authors make mention of dropsy in connection with abnormal conditions of the kidneys.

J. B. Morgagni, Epistle 42, *De Sedibus et Causis Morborum*, describes the case of a dropsical patient who died suddenly, and whose body he examined. "Renis utriusque structura intima confusa apparuit"; and, in Epistle 40, he anatomises the kidneys of an old woman. "Ren uterque inæquali erat superfici et maculis albis hic illic variegata." Morgagni notices, in Epistle 41, art. 4, a case of acute renal dropsy, provoked doubtless by exposure of the body to cold in the treatment of itch. Morgagni writes: "The kidneys were larger than normal." (I remember seeing an exactly parallel example in Vienna in Hebra's clinic.) The itch was treated by an ointment rubbed into the skin: suppression of urine and vomiting followed, pain in the left lumbar region, general dropsy, and death. Granular kidneys and large white kidneys had therefore been discovered before Bright wrote; while Avicenna, in 1164*, was certainly before him in distinguishing between the

dropsies consequent upon disease of the liver, and those which followed upon disease of the kidney.

It is to Cotugno, however, in 1770 (*De Ischiade Nervosa Comment.*, Viennæ, p. 24-25), that we are indebted for the discovery of albumen in the urine of dropsical persons, which he attributed to the passage of the dropsical effusion over into the urine, and regarded, unfortunately most incorrectly, as nature's mode of resisting and repairing disease.

In 1798, Cruickshank advanced matters a step further (*vide Rollo, Cases of Diabetes Mellitus*, chapter vi, London), by recognising the fact that in some cases of dropsy albumen did appear in the urine, while in others it did not.

Darwin, *Zoonomia*, vol. i, p. 467, third edition, London, 1801, noticed a form of diabetes in which the urine was albuminous, and coagulated with heat occasionally; a condition preceded, and he thought occasioned by, general dropsy.

In 1809, Dr. Latham the elder, in a work published by him, *Facts and Opinions concerning Diabetes*, notices a case in which the urine, ceasing to contain sugar, continued to be excessive in quantity, and became albuminous.

Dr. Wells, whose Observations on the Dropsy which succeeds Scarlet Fever were published in the *Transactions of a Society for the Improvement of Medical and Chirurgical Knowledge*, vol. iii, pp. 16 and 194, may be fairly regarded as the pioneer who probably guided Dr. R. Bright to his clinical investigations upon the connection between renal disease and dropsy. Wells it was who pointed out that the urine after scarlet fever contained both blood-colouring matter and blood-serum; and that, even when scarcely abnormal in aspect at all, it might contain sero-albumen, recognisable by its coagulability both with heat and with nitric acid. Out of 138 cases of dropsy after scarlet fever, he discovered serum, as he rightly enough calls it, in the large proportion of seventy-eight times; and, later on, pursuing his inquiries further, Dr. Wells observed that other cases of general anasarca were associated with renal disease and coagulable urine. He seems, too, to have completely forestalled Dr. Bright in his analysis of the clinical symptoms, having observed that in this variety of dropsy sharp pains in the loins and limbs sometimes preceded as well as attended the dropsy, and that the pulse, far from signifying general weakness, was often full and frequent. The case recorded by Wells, of a soldier, aged 47, who died of dropsy, complicated finally by an inflammation of the lung, whose kidneys he found harder than normal, their cortical parts being thickened, and structures generally altered by deposits of coagulable lymph through their substance, is probably the first distinctly diagnosed case during life of chronic renal disease. Wells's work in this direction was eminently philosophical. He discovered albumen first in the urine of post-scarlatinal dropsy; afterwards in the urine voided in other species of dropsy connected with pathological states of kidney; then he examined the urine of persons in apparent health; and again occasionally lighted upon the presence of albumen in it. He ascertained that blood-serum was discoverable in the urine in many forms of chronic as well as of acute disease; and discovered it once in the urine of a person who enjoyed the aspect of health, but who subsequently died dropsical.

In 1813, Dr. John Blackall published a volume, *Observations on the Nature and Cure of Dropsy*, which ran through several subsequent editions. The most frequent cases of renal dropsy which he records were the forms following scarlet fever, and the cases of acute diffuse nephritis determined by exposure to cold and wet in persons who were pursuing a course of mercury. He surmised, but failed to prove, that the normal amounts of urea were retained in the system in these cases; and, although he made out that the kidneys were diseased in an unusual proportion of the cases, he was evidently biassed by the various other inflammatory lesions, of which, as he writes, "the whole system bears the greatest marks"; and attributed the affection less to the kidney-lesion than Wells had done, and more to a wide-spread inflammatory general disposition. This theory of his led him to recommend free blood-letting and depletory treatment.

Dr. Scudamore, in his treatise on *Gout* published in 1823, insisted on the clinical and prognostic importance of albumen occasionally found in the urine of dyspeptic and gouty subjects, and noticed that these persons were of a peculiar nervous habit, and micturated frequently. More than this, he pointed out that, although no dropsy attended on these symptoms, the urine departed from a normal standard not only in containing albumen, but by holding less urea, less uric acid, and less salts altogether than it should do. It was an imperfect secretion, he wrote.

M. Andral in 1826 published, in his *Clinique Médicale*, tome iii, p. 567, a case of dropsy without affection of the heart or peritoneum, in which the kidneys were the sole organs diseased. His description of

* Avicenna, *Libri in re Medicâ omnes* (lib. 3, fin. 14, tract. 4, cap. 4). de Hydro-pisi, p. 769, in foliis Venetiis. "A renibus vero non solum fit communicantia noxæ per se, sed ex accidenti, si aquositatem non purgant, unde multa remanet in venis; atque sanguis aquosus et excolitur serum."

these granular kidneys is very precise. Thus, he writes, the external cortical substance, and a part of the tubular (*i.e.*, medullary) portion, consisted chiefly of white granular tissue, and appeared divided up into little masses or grains which stood out distinct from the natural red tissue of the kidney. The cause of death in this case was double hydrothorax; but this he referred to the original or primary renal lesion.

In 1827, Dr. R. Bright published his *Reports on Medical Cases*; and in the same year, and probably entirely uninfluenced by his writings, M. Barbier of Amiens published in Paris his *Précis de Nosologie et de Thérapeutique*, in vol. i, p. 410, in which he describes Bright's small granular kidney as a fact well known to him, writing: "On rencontre souvent les reins d'une petitesse remarquable; leur volume réduit au tiers on au quart de ce qu'il devrait être." He calls the affection "oligotrophie", and adds: "La sécrétion urinaire est toujours (?) notablement diminuée, il survient souvent un œdème général." He gives the case of an old woman in the Hôtel Dieu as an illustration of this affection, and notices that, with the exception of a heart "légèrement dilaté, les autres appareils étaient en bon état". A sudden pleurisy was also the final cause of death here. At p. 553, we find a chapter with the heading "Sclérisie des Reins", in which he shows his intimate acquaintance with this affection in its late stages, and its relation as a cause, often overlooked, of a rebellious form of anasarca, in which the blood-serum had a more milky colour than was normal—leucophlegmasia with renal sclerosis.

Dr. Richard Bright's first publication appeared in 1827; it had been led up to, as all great epochs in the history of medicine have been, by study as well as by clinical observation. Blackall and Wells had already established the importance of albumen in the urine as a symptom of dropsy. The distinguishing feature of Bright's volume is its careful reasoning and its modest inferences from facts, put forward after patient investigation of them. He heads the first chapter very tentatively, "Cases illustrative of some of the Appearances on the Examination of Diseases terminating in Dropsical Effusion". The cases are narrated, the clinical symptoms described, and the *post mortem* appearances dwelt on. The connection of diseased kidney with certain dropsies is pointed out; and the alterations in the structure of the kidneys found in the bodies of those whose deaths had been preceded by dropsy and albuminuria are sketched by a masterly hand. He distinguishes a dropsy in which the kidney is found diseased from a dropsy in which the liver is diseased; but he is far too cautious to advance to inferences unjustified by the facts before him, to talk of renal dropsy or of primary renal disease as the cause of dropsy. He speaks of the coincidences—the associated facts. By him, in the first instance, the structural changes in the kidney are attributed to certain injurious influences which, acting on the stomach or the skin, disturb the renal functions, either by disordering the circulation through the kidneys, or bringing about a state of decided inflammation in them. Further on, he writes that he thinks his observations almost authorise him to establish three varieties, if not three completely separate forms, of diseased structure; but he does not pin himself down to these three typical forms. He thought his third form might be an advanced stage of the same essential process which produced the second; and he distinctly notices other conditions of kidney—a preternatural softness of the organ, associated with similar flabbiness of the liver, spleen, and heart, as a pathological condition which led to albuminuria; and describes a separate category of cases, in which the kidneys were firmer than normal, and where the tubules were blocked up. I wish to point attention to his caution in making varieties, and to the conciseness with which he attributes the renal structural changes to wide-spread influences, which, acting either through the stomach or the skin, disordered the renal circulation and its functions.

After all the work that has been expended in the closer investigation of the minute anatomy of the different diseases of the kidneys, and all the clinical observations which have been published in the last fifty-four years upon the same subject, the questions whether there be one or more varieties of diffuse renal disease, and what is the real first cause of the renal degenerations to which he called special attention, remain much where he left them.

According to Bright, the one category of cases comprises yellow-white kidneys, nearly of normal size, at first with pyramids paler than should be, spotted yellow intermixed with grey throughout their cortical substance, and which, at more advanced stages, acquired a more tuberculated aspect, presenting elevated knobs which were paler than the parts surrounding them, and into which no injection-fluid thrown into the arteries would enter. This form was encountered most often in cachectic phthisical individuals, and appeared to be determined by exposure to cold and initiated by hæmaturia. The other category of cases presented the following pathological aspect. The kidneys had a

generally spotty granular appearance, "looking as if fine grains of sand had been deposited in them". The organ was sometimes larger, sometimes smaller, than normal. This appearance he attributed to an abundant interstitial exudation of an opaque material. The entire surface of the kidney became, later on, roughened and covered with countless small nodules of the size of a pin's head, some yellow, some red, some bluish-coloured. The organ was hard and tough, and appeared contracted in every part. The interstitial deposits were less distinct; and the pervading colour was a red-grey, sometimes deeper, sometimes lighter. This kind of kidney was found principally in persons who lived irregular lives, abused alcohol; and the injurious influence underlying it is vaguely hinted at as some disorder of stomach or digestion.

The writers who followed Bright, amongst whom in Great Britain the most eminent were Christison, James Gregory, Osborne, Copland, Elliotson, Graves, and Willis, added clinical information of no inconsiderable value; but some of them busied themselves over-much in controversy upon the etiology of the new disease, and neglected investigating the nature of its pathology. Thus we find doctors differing very early, and ranging themselves in two hostile camps; the one as humoropathologists, teaching that the disease was general, and commenced in a vitiated state of the blood, before the kidneys suffered; the others maintaining that the kidney-disease was primary, and led to the impairment and mal-constitution of the blood.

Dr. Bright, in the publication of his second volume, which appeared in 1831, having established upon irresistible evidence the coincidence of the three facts—dropsy, albuminuria, and special pathological changes of the kidneys—inferred that the renal lesion ought to be regarded as the first cause, or entity of the disease, and the dropsy and albuminuria as the consequences of it.

Christison and James Gregory stood by Bright, and they further advanced our knowledge—Christison by careful clinical examination, both of the urine and of the blood-serum, in various stages and varieties of renal disease. The discovery of urea in the blood, and several estimations of its quantity in renal dropsies, were made by him in some cases of albuminuria; and he was led to accept the idea—first put forward by MM. Prevost and Dumas, founded on experiments made by them in extirpating the kidneys of animals—that urea was not generated by the kidneys, but separated by them.

Christison proved to demonstration the low specific gravity of the serum of the blood that attached to chronic renal disease; confirmed the associated hypertrophy of the heart which Bright had noticed; discussed the essential and non-essential symptoms; showed that general anasarca, although a very frequent, was no necessary symptom of diseased kidney; called attention to pulmonary catarrh, emphysema, and hæmorrhagic apoplexy, as more frequent complications than inflammations of the serous membranes; and pointed out the tendency to death by coma and so-called serous apoplexy, often discovered in these cases, when the necropsy presented congestion neither of the brain nor of its membranes.

Dr. J. Gregory's observations on diseased kidney (*Edinburgh Medical Journal*, 1831, vol. xxxvi, p. 318), connected with albuminous urine, are quite equally remarkable. He fully recognised the fact that the urine might be albuminous in certain disordered states of the system, unconnected with any special pathological alteration of the kidneys. "But", he writes, "when the urine is coagulable, and at the same time decidedly low in density, and below the natural standard in quantity; and when this state of urine has existed for some time, in a more or less marked degree; and when it is accompanied by dropsical effusion, in some of its forms, particularly slight but obstinate œdema of the extremities and face; or when, in the absence of dropsy—by no means a constant symptom—there is intractable vomiting or diarrhœa, we have evidence of organic disease of the kidney, upon which we may rely with much confidence."

Dr. Elliotson, Dr. Copland, and Dr. Graves contended against the prominence given to the renal changes. According to them, the whole system, and especially the blood, was first disordered. Graves, in the *London Medical Gazette*, December 1831, regarded the albuminuria as the cause of the renal changes; while all were agreed that the prognosis of these cases turned less upon the quality of the urine, and the quantity of albumen in it, than upon the associated general symptoms.

In 1838, Dr. Robert Willis published a work on *Urinary Diseases and their Treatment*. It was a work that deserved translation, and it was translated into German by Heusinger, and published at Eisenach, in 1841. Dr. Willis divided albuminous urines into sero-albuminous and fatty albuminous, and regarded the amount of fatty matter contained in any urine as some measure of the gravity or extent of renal degeneration. He further entertained some vague chemical ideas that the albumen in urine might be regarded as a substitution-product from urea (*vide page 121*). In his book, reference is made more than once to Bright's

disease, as a new discovery. Dr. Willis's book, read at the present time, offers little of interest regarding the diffuse diseases of the kidney; but there was a certain order about it that recommended it to book-writers; and it is probable that its appearance in Germany introduced Bright's observations to German readers, and stimulated many to read his clinical reports.

It was in 1838, also, that Martin Solon published in Paris a work on *Albuminuria or Dropsy caused by a Disease of the Kidneys*; and to him in England we owe the vague general denomination of albuminuria for a variety of renal affections, some of which were, but many of which had no claim whatever to be, classed as the kidney-disease which Bright had clinically portrayed.

M. Rayer's work, *Traité des Maladies des Reins*, was not yet published, but the materials for it must have been forward in Rayer's hands, for as he himself writes, vol. ii, p. 566, "My first researches on renal disorders were begun in 1830."

As Rayer justly says, to group together, under the head of albuminuria, affections so different in nature and issue as M. Martin Solon did, was practically useless. Albuminous urine is a symptom, not a pathological entity. Evidently there were many passages-at-arms between M. Martin Solon and M. Rayer at the Royal Academy of Medicine; the one maintaining his *néphrite albumineuse*, with six different subforms; the other, his *albuminurie au premier, second, et troisième degré*; or, 1. Sans lésion rénale; 2. Avec lésion rénale; 3. Avec hydropisie; 4. Avec les productions granuleuses du Bright; 5. Avec dégénérescence variée du tissu renal et productions accidentelles.

To Rayer, however, the thanks of all who study renal diseases must eternally attach, for a work quite unparalleled in the annals of medicine for research and clinical acumen. Its weakest part is just Bright's disease—the acute and chronic forms of diffuse nephritis—and here it falls short, because, at that time, neither the minute normal nor the pathological anatomy of the kidney had been much investigated in Europe.

Hitherto, the disputed points had been a primary renal or a primary blood disorder; but, now that the German observers—up to this date singularly indifferent to Bright's discovery—took up the matter, the nature of the renal lesion began to be closely sifted by the microscope. Was it an inflammatory process, a fatty degeneration, a steatosis, a fibrous degeneration, or fibrosis? Was it one disease from first to last, with various stages, or were there several distinct varieties, each with its own separate clinical history?

Passing over, as we may, with scant notice the early pathological observations of Gluge, Valentin, and Henle, Vogel, Canstatt, and von Siebold, our attention is arrested by Reinhardt's work, published in the *Deutsche Klinik* (von Götschen), November 5th, 1849, who attached all the pathological states of kidney described by Bright to inflammatory processes. He gave the name of diffuse inflammation to the changes in question, because the exudation poured out showed little disposition to organise, and because it extended widely through the affected organ. It was a croupous form of inflammation, because casts came away from the tubular structures; it was an inflammation that pursued various courses, according to the causes that induced it, and the individual it invaded; but he did not regard the various forms of kidney figured by Bright as the result of one single process of disease, but of several successive invasions. Like every other inflammatory process, it might come under observation at different stages of hyperæmic congestion of exudation, with fatty degeneration of epithelium, of new growth of connective tissue, with ultimate contraction like that of scar-tissue.

It is not to be supposed that the professors of pathology in the Berlin and Vienna schools had overlooked conditions so obviously abnormal as the kidneys of Bright's disease presented. Rokitsky, in his textbook of *Pathological Anatomy*, 1842, described eight forms of morbus Brightii, of which the lardaceous kidney was the last; but the clinical symptoms attaching to these were not understood; for the minute anatomy of the kidney, and the physiology of the urine-secretion, had been hitherto only imperfectly studied.

The first important step in advance was Mr. Bowman's philosophical paper on the Structure and Use of the Malpighian Bodies of the Kidney, published in 1842 in the *Transactions of the Royal Society*, which described the minute anatomy of the organ with great care. From the facts before him, Mr. Bowman inferred that the glomerules separated the urine-water, and the secreting tubes and cells the urine-solids; and the situation of the tufts incorporated at the terminals or beginnings of the tubules, indicated them, as he thought, to be an apparatus contrived for washing the more solid secretion out of the renal epithelium. Thenceforth, the study of Bright's disease advanced *pari passu* with anatomical investigation and physiological experiment. To follow it step by step would require a longer review than we can afford to write,

although we propose to glance briefly from henceforth at some of the important stand-points, as these have been in succession reached.

For many years in England, Bowman's views were accepted without a doubt, and may be certainly regarded as the foundation-stone upon which the English physicians and pathologists based their doctrines of renal disease.

In November 1845, Dr. G. Johnson published in the *Medico-Chirurgical Transactions* his earliest communication on the Minute Anatomy and Pathology of Bright's Disease (*vide* vol. xxix, 1846). He found that the granulated or mottled aspect of the kidney, associated with albuminous urine and dropsy, was due to an inordinate amount of fat collected in the renal epithelial cells; and he reasoned, correctly enough, that such a distension and infarction of the tubules must encroach upon the intertubular capillaries, retard the circulation through these networks, and lead to engorgement of the Malpighian tufts. Fatty degeneration of the renal epithelium was, he thought, the commencement and essence of Bright's disease; effusion of blood and blood-serum in the urine was the result of abnormal blood-pressure, secondary to the infarction of the tubules.

Even at this early period, Dr. Johnson distinctly taught that the kidneys described by Dr. Bright could not be accepted as different stages of the same disease. Bright's small red granular kidney had little in common with the large white smooth one; and, if the name of Bright's disease was to be retained for a renal degenerative process, which began and progressed by fatty metamorphoses, the white kidney must be separated from the atrophic organ.

Dr. Johnson's communication evoked a notable rejoinder from Dr. Quain, which appeared in the *Lancet* for November 1845, p. 594. Quain writes that, "in more than fifty specimens of this disease examined by me, the fatty condition of the kidney was, in one instance only, sufficient to attract much attention." In the large proportion of cases, he found cacoplastic lymph, either in the form of nucleated cells, or of simple granular matter, or of a deposit that he observed assuming distinctly filamentous or fibrous characters. He assigned the seat of the deposit to the parenchyma of the kidney, external to the tubes, and observed granular matter contained within the tubes themselves. He inferred that congestion preceded the deposits, and that the changes in dispute were from the first inflammatory. He makes three forms of kidney-disease the several outcomes of these different forms of deposit or exudation: 1. The simple enlarged mottled kidney; 2. The truly granular or atrophied kidney; 3. The large, flabby, fatty-looking kidney.

Dr. Johnson's views on fatty degeneration received complete sifting and plain answer by Professor Virchow in his *Archiv*, Band iv, s. 260 (1847), where the inflammatory nature of the initial changes in Bright's disease was clearly enunciated. Virchow further distinguished between simple tubular catarrhal and parenchymatous inflammation, the former recovering completely without further hurt, the other having possible issue in interstitial or glandular hyperplasia.

In reviewing, however, what was done at this date, it would be unjust not to mention a very elaborate paper communicated by Mr. Toynbee to the *Medico-Chirurgical Transactions*, in 1846, on the intimate structure of the human kidney. Toynbee was most successful in his injections, both of the tubules and of the arteries. Dr. Bright had himself furnished him with a great variety of kidneys in several stages of disease, and very good use he obviously made of them, as his drawings and text prove. He was the first to establish distinctly the existence of intervascular spaces (*Med.-Chir. Trans.*, vol. xxix, p. 304) of no inconsiderable size, situated between the blood-vessels and tubuli, and occupied by a substance he named parenchyma. Ruych had described this as a cellular network, connecting the vessels together. Toynbee recognised the importance of this intertubular parenchymatous network of cells in diseased processes. It may be seen that his drawings of the tubuli uriniferi (*vide* figs. 2, 6, and 8), entirely confirm the latest modern views (Dr. Klein) on the size and contours of the tubes. He showed how in the second stage of Bright's disease, when the primary congestion of the organ subsided, the swelling and dilatation of the tubuli compressed the intertubular capillaries, while the afferent arteries to the Malpighian bodies became enlarged to eight or ten times their normal dimensions, and proportionally varicose, and how, in the third stage, the parenchyma became hard and appeared composed of elongated stellate cells having fine thread-like prolongations. His views, therefore, formed quite independently of Dr. Johnson, tended to strengthen those of the latter, in his separation of the large anæmic fatty kidney from the small granular vascular one.

In 1847, Dr. Johnson's second communication to the *Medico-Chirurgical Transactions* was published. It discussed the inflammatory diseases of the kidney, which he divided into two classes, traumatic

and constitutional. The lesions, which he attributed to a constitutional cause, some abnormal condition of the blood, he subdivided into four different types or forms: 1. An acute desquamative nephritis; 2. A chronic desquamative nephritis; 3. Simple fatty degeneration; 4. A combination of fatty degeneration with desquamative nephritis. He showed that in all these forms morbid materials were deposited in the tubules, and washed out of them again, forming casts (Franz Simon's fibrinous threads), which were to be of the highest importance as indices for treatment and in prognosis.

In the same volume of the *Transactions* (vol. xxx, 1847) appeared a remarkable paper from the pen of John Simon, who thought it indispensable for correct nomenclature, that the name of Bright's disease should be discontinued. He is convinced that there are at least two forms of disease confounded together under this term, for he too, like Johnson, is an early dissident or dualist. He separates one form of kidney-disease from the other by the nature of the inflammation which subtends it. One is an ordinary subacute inflammatory process, the other a scrofulous degeneration.

Subacute inflammation of the kidney might, according to his views, be provoked by exposure to cold, by rheumatism or by gout, by intemperance, by the circulation of various fever-poisons in the blood. The products of inflammation, poured out into the tubes, led to blocking and bursting of them, and to liberation of inflammatory exudation as well as of free renal epithelium cells into the parenchyma of the organ; the exudation materials subsequently underwent contraction; the free renal cells developed into cysts. Thus was brought about the small, red, granular kidney containing multiple cysts.

The scrofulous degenerative disease, however, as it had a different etiology, so, too, pursued a different pathological course, which consisted in the successive deposition of fatty materials in the glandular substance, which slowly accomplished its entire disorganisation, and resulted in a large white or mottled kidney. "The mottled kidney," he writes, p. 158, "in an infinitely large proportion of cases remains large and mottled to the end."

That the temperament and health of the individual modifies the course taken by disease in all his organs, who shall gainsay? But the distinctions he drew admit of fixing by no hard and fast lines, and, therefore, as grounds on which to base a classification, do not recommend themselves.

But among the many valuable and most suggestive ideas scattered through this most careful paper, the following passage proves how thoroughly he realised the fact that the peculiar shape and length and alterations in calibre of the tubuli uriniferi modified the final result of inflammatory processes involving them. Thus (p. 142) "the complexity of the tubules, the narrowness of the canals, render them especially liable to be embarrassed by changes in the physical qualities of their secretions.....the delay, accumulation, and obstruct action of which suffice to derange the whole microcosm of the (gland) in which they occur."

Even at this early date the thickened state of the renal vessels had attracted attention, as well as what Bright had observed, the associated hypertrophy of the heart. It is not very easy to ascertain who was the first to perceive that the arterial walls of the renal vessels became thickened. Toynbee noticed the fact in his injections of Bright's kidneys, published in 1846; and Dr. Johnson, in his third communication to the *Med.-Chirurgical Transactions* in 1850 (vol. xxxiii, p. 107), writes to this effect. The changes of the secreting cells involve imperfect elimination of renal constituents from the blood; the nutritional changes do not go forward properly, and this accessory circulatory force becomes impaired. Hence the tendency is for the blood to delay in the capillaries and to require additional pump-force from the heart to drive it forward, when what happens is, that the heart becomes hypertrophied, and the walls of the arteries also.

The same fact is dwelt upon by him later on, as a most important factor in the development and progress of renal disease. It is only necessary to call attention to the matter here, as a part of the history of Bright's disease; its importance will claim notice later on.

At this date, *i.e.*, about 1850, Martin Solon's vague name of albuminuria for acute and chronic renal disease, was in England, as in France, creeping into general use; it recognised a fact, and avoided a difficulty; it implied that the kidneys performed their function faultily, and hazarded no diagnosis upon the nature of the lesion in them. It left room for an open prognosis to be drawn from observation of other symptoms; it might, or might not, be a serious symptom itself. Bright's disease was a term as yet of very uncertain value. English physicians were quite undecided whether it should be held to comprehend one uniform pathological state of kidney, or a variety.

Dr. Owen Rees now published (1850) a volume on *The Nature and Treatment of Diseases of the Kidney*. In this he thoroughly sifted the

subject, in what Bright's disease consisted, and to what it should be restricted to—namely, degenerative changes of the kidney, which were the result of past or present inflammatory processes.

After ably showing (p. 40) the fallacy of the argument that a general blood-disease should not be found guilty of inducing degeneration or inflammation in one special organ, he writes, "but so far as our present knowledge extends, it is in the tissue of the kidney itself that we see those first departures from a normal state which produce albuminuria. Many of the changes observed in the blood may undoubtedly be traced to the condition of the kidney." Dr. Rees was the earliest writer to point out that urine, with excess of earthy phosphates in it, gave a copious white deposit on being boiled, which closely resembled albumen, and had often been mistaken for it. He also showed how to obviate error by the well-known reaction with nitric acid. He was too, I think, the earliest to notice the frequent desire to rise and pass urine at night as a symptom of Bright's disease (p. 59), and the hard, wiry pulse, less elastic than in health, and tortuous, [which, if connected with a pallid face, is, as he says, very suggestive of the nature of the malady.]

In 1851, Frerichs's monograph, *Die Brightsche Nieren-Krankheit*, was published in Germany, and carried throughout Europe the name and discoveries of the great Guy's physician, who had linked together albuminous urine, general dropsy, various pulmonary affections, asthma, bronchitis, and pleurisy, uræmic symptoms, and apoplexy, with a peculiar and insidious pathological degeneration of the kidney, and showed how the kidney-disease led to an alteration of the blood, and this alteration of the blood to an hypertrophy of the heart, wholly independent of any disease of its valves.

New and more comprehensive views upon inflammation than those which had hitherto chiefly emanated from the Vienna school were advancing from the north of Germany. The era of fluxions and exudations, catarrhal, croupous, and fibrinous, was drawing to a close. Could the pathological alterations, described by Bright as taking place in the kidney, be left to fulfil the old conditions of an inflammatory process? Could it be interpreted by them?

Frerichs describes the pathological events as succeeding each other in the following order. The mischief began in the kidney by a first stage of hyperæmia and exudation into the parenchyma of the gland; it was continued (his second stage) by various metamorphoses which the exudation underwent; it terminated (his third stage) by retrograde changes and atrophy of the glandular substance. One important feature of the second stage, which he illustrates by a woodcut, is the varicose dilatation of the secreting tubes, sometimes, as he says, to twice or three times their natural size (p. 28); some portions of the tubes retaining their cell-linings in an apparently normal state, others presenting altered and fatty cells in them, and others, again, being left apparently quite denuded, as Dr. Johnson had described them. He admits that the second stage was that which most frequently fell under observation. He makes an acute and a chronic form of the disease. At p. 58, he shows the objection to Dr. Johnson's inference, that the nature and extent of the degeneration can be diagnosed by the casts, because the diseased process exists in different stages at the same time in the same kidney, and because every variety of cast may be present at one and the same time. He considers the amount of albumen in the urine a measure of the intensity of the exudation-process, and explicable upon the anatomical changes in the gland, much of which is destroyed. As to the effect of the removal of renal epithelium upon the escape of albumen, he pronounces no definite opinion. According to him, the immediate effects of renal disease upon the system are: impoverishment of blood; increase of organic materials in it from impurities, which ought to have escaped, remaining combined in the blood. Among the symptoms to which he calls special attention—and his symptomatology leaves little to be improved upon—he notices the occasional follicular ulcers of the colon (p. 103), and the presence of carbonate of ammonia in the blood.

The great novelty of his work was his ammoniæmia theory of uræmia, which may be stated in few words. Urea, he said, as experiments led him to believe, might circulate in great excess in the blood, but would provoke no toxic symptoms, unless it underwent decomposition into ammonia carbonate; and the presence of some special ferment in the blood, as well as of urea, was requisite in Bright's disease for the production of uræmic symptoms. The proclivity of any patient who had renal disease to uræmia could be estimated by the amount of free ammonia in his blood, and its great excess easily be rendered apparent by a glass rod dipped in hydrochloric acid fuming freely when brought into contact with ammonia-laden breath. The original experiments were faulty, and his inferences were not justified by his facts. They obtained very little acceptance. Ammoniæmia has been long since relegated to the limbo of unproven physiological doctrines.

Frerichs' book was strongest in its clinical descriptions of the symptoms marking the different stages of renal disease; these are sketched by a masterly hand.

In 1852, Dr. Wilks published an article, entitled Cases of Bright's Disease, in the *Guy's Hospital Reports*, 2nd series, vol. viii. He began by expressing his preference for the name of Bright's disease over that of Albuminuria; since renal disease, he found, might exist and no albumen escape in the urine, and albuminuria might occur temporarily without depending upon any such lesions as Bright had described in the kidney. Bright's disease, he acknowledged, was still very imperfectly understood, pathologically or clinically; but certain well-observed structural changes in the kidney, accompanied by a regular train of symptoms and secondary pathological phenomena, might be vouchsafed to indicate it. He criticised Frerichs' book, and naturally assailed the weak point in his argument. If the small granular kidney was the final stage of one uniform process of disease, successive inflammatory congestions, exudations, and subsequent degenerations and contractions, how was it that so few examples of the intermediate pathological states were encountered? Why was it, that no single case was mentioned in which the symptoms betokening the large inflammatory kidney could be traced, gradually altering into such as characterised a small granular kidney? or that no case of ascertained small granular kidney was observed as having been preceded by acute symptoms? At p. 238 he writes: "In chronic granular kidney, the urine is often in good quantity, containing no deposits, and may or may not be albuminous." Dr. Wilks pronounces himself as a very positive dualist, and discriminates two principal forms of Bright's disease—the large white and the small granular—and then describes the rarer or lesser varieties, the mixed forms, and secondary forms, of later writers. He distinguishes the red swollen coarse kidney of passive venous hyperæmia; the dense white fibrous kidney (which I shall hope to show hereafter to be the kidney of obstructed urinary outlet); and the simple fatty kidney of phthisis. He is the first author I have read who points out plainly that the large white kidney may have two modes of commencement: either by acute general dropsy, or quite insidiously. He is the first to speak of granular kidneys as indicating senility; to notice how (*vide* p. 256) "the older the patient is, the more liable is he to granular degeneration of the kidney"; and he remarks upon the thick tortuous radial artery, the general anæmia, the characteristic pale urine, and the desire to micturate frequently, as well as the tendency to death by apoplexy or uræmia, in this chronic malady. He compares the changes in the large white kidney to bronchitis in the lungs, which may be recovered from entirely, or may pass on, by extension of the inflammatory processes through the parenchymatous tissue of the organ, to degenerations analogous to those which take place in broncho-pneumonia.

His description of Bright's disease leaves nothing to correct, and little to add; but he is not much captivated (*vide* p. 274) by Johnson's theory of the mode in which the albumen escapes from the blood, attributing the albuminuria, straightforwardly, to obstruction of the circulation through the tufts and capillaries, and not to its transudation through the tubes because of their being denuded of cells.

In 1852, appeared Virchow's pamphlet, *Ueber Parenchymatöse Entzündung*. This form of inflammatory change in the kidneys is thus described by him: the elements of which the actual tissues of the organ are composed swell up, the cells become cloudy, less transparent and more granular, as well as more friable, than they should be. The possible issues are in one of two directions: 1. The epithelial elements may soften down into a proteinous jelly or pulp; 2. They may become milky and undergo fatty metamorphosis. Parenchymatous inflammation in the kidney, he insists, does not exclude the simultaneous occurrence of interstitial hyperplasia. Catarrhal, croupous, and parenchymatous exudation may be combined together, and will then lead to the highest degree of renal degeneration.

Virchow's simple catarrhal affection of the tubuli appears to correspond with Johnson's acute desquamative nephritis; and both allow that this admits, in its slighter grades, of complete recovery. Virchow's croupous nephritis is a graver grade of catarrhal inflammation, in which fibrinous exudations are poured out into the tubules and block them up; and Virchow advises the attachment of the name of Bright's disease, not to any temporary or transitory affection with albuminous urine, but to those graver and more extended inflammatory changes, which, starting from parenchymatous inflammation, ultimately invade every elemental structure of the kidney, and entail its complete degeneration.

Johnson and Virchow are agreed in what they are describing and what they would call Bright's disease; but they differ widely in the terms which they employ to represent the pathological process, and in the method by which they interpret the phenomena. Johnson is a trifle too allegorical with his desquamative nephritis, and Virchow stretches the old-

world notion of inflammation prevalent at that time to bursting point with his parenchymatous swelling.

Traube, in his volume on the connection between renal and heart disease, broke fresh ground in 1856, when he distinctly separated the cardiac kidney, *i.e.*, the kidney of passive renal hyperæmia, from the kidney of Bright's disease or primary kidney-disease, and showed that, while valvular heart-lesions entailed kidney-disease in many instances, chronic kidney-degeneration, and especially Bright's atrophic kidney, compelled heart-hypertrophy as an almost inevitable consequence. In this work, Traube summed up, with the master-hand of a clinical teacher, the mode of distinguishing the primary from the secondary disease, writing: "In both, the urine is albuminous; but when the renal degeneration is primary, and the cause of the heart-hypertrophy, and the hypertrophy is adequate to the renal defect, the urine is copious, pale, and generally of low specific gravity, and the amount of albumen in it variable (but seldom considerable); whereas, when the renal degeneration depends upon passive congestion secondary to heart-disease, the urine will be dense, scanty, and high-coloured, and its albuminous contents large in amount." His pathological description of the two kidneys is equally good. "The kidney secondary to heart-disease is large, tough, and extremely blood-gorged in its vascular zone; while the kidney whose degeneration has evoked wide-spread complications and changes secondary to itself as events, although not in importance, will be found atrophic, pale, tough, and granular."

Traube's inferences were criticised by many writers, and with some skill by Bamberger, who, in an article published in Virchow's *Archiv*, Band xi, 1857, p. 12, showed that valvular lesions of the heart (those remarkable forms of accretion of fibrinous vegetation), not only were no rarity in, but formed really a very common incident and complication of, the renal disease (as later experience has abundantly proved, they especially occur in the large white kidney-disease of short course and excessive albuminuria); and that these lesions, and not the impediment to the circulation in the kidney, ought sometimes to be held guilty of the cardiac hypertrophy. He concedes, however, the main issue, Traube's real hit, that in some cases of chronic renal disease the heart was found greatly hypertrophied without valvular disease or any other obvious cause, and for which he was the first person to offer a mechanical explanation.

Meantime, the English observers and physicians were not idle, but, having arrived at the conception of Bright's disease as a renal degeneration, presenting itself in several varieties with distinct pathologies, clinical symptoms, and issues, were directing their attention more to the best mode of distinguishing these separate forms during the patient's life, and at advancing diagnosis, prognosis, and treatment—*vide* Dr. Basham *On Dropsy and its connection with Disease of the Kidneys* (1st edition, 1858), and Dr. Dickinson: "Two essentially distinct conditions of Kidney, giving rise to what is called Bright's Disease" (*BRITISH MEDICAL JOURNAL*, 1859). By both these writers, good use was made of the microscope in investigating the sediment of the urine, as a clue to the changes taking place in the kidney, and in examining the kidney, in the hope that it might explain how its degeneration had been brought about.

It is an easy and an invidious task to look back now, and say how much of this labour was profitless; how few of the inferences made by Basham as to diagnosis, upon the appearances of renal casts, have been confirmed; and how little light the earlier microscopical examinations of renal disease really threw upon the changes that took place in the tissues of the kidney, and the order in which they succeeded each other. The anatomy of the organ still was very imperfectly ascertained; and as with the lung, so with the kidney, to read the course of disease backwards to its beginning, from the appearances found at the death-stage, is to court failure and invite error.

Dr. Wilks's writings, and the manner in which he had likened renal to pulmonary disease—the analogy he had drawn between bronchitis and catarrhal nephritis, and between bronchopneumonia and catarrho-interstitial renal degeneration—led Dr. Basham on to see further resemblances between tubular casts and sputa; things, of course, which admit of no denial, but advance actual knowledge infinitesimally little.

Those who refer to Dr. Basham's work will see that, at this period, an opinion of the extent and gravity of renal degeneration, instead of being based, as the older writers—Christison and Gregory, and Osborne—had insisted that it should be, on the estimation of the amount and density and solid constituents of the urine as the measure of the capacity of the kidney to perform its function (as Bartels put it later on) ran grave risk of being hurriedly inferred from casts found in the sediment of the urine, which were valuable, no doubt, as additional evidence, but far from being all-sufficient in themselves to base an opinion upon.

In 1859, we find Traube, in his *Klinische Untersuchungen* (page 969), noticing the association of amyloid degeneration of the kidney with albuminous urine. Renal casts passed in the urine during life, and plugs loaded with fatty detritus were found blocking the tubuli uriniferi after death. The kidney presented a waxy appearance; the degenerative change was nearly entirely confined to the blood-vessels; no appearances suggestive of parenchymatous inflammation were perceived, or led him to attribute the plugs or casts to active changes of or in the renal epithelium. Fatty degeneration of the renal epithelium might, therefore, be induced by other causes besides inflammation; and in amyloid, perhaps, as in some other cases, should be attributed to a kind of necrosis.

Casts, as Frerichs had shown, neither by their size, nor their quantity, nor their characters—whether full of cells, or of fat, or of granular matter, or of blood-cells—could be accepted as evidence of the actual state of the kidney; although there was a great unanimity of opinion among observers that fatty casts were signs of ill-omen, and that sediments, which contained large hyaline casts, and numerous white (or compound granular) cells, associated with botryoidal clusters of free nuclei (*vide* Dr. Basham, fourth edition, page 130), usually indicated a most intractable, because most widely diffused, form of renal degeneration.

Differentiation was the order of the day; the pendulum which Frerichs had forced back to Bright's last-issued idea, that his disease was, essentially and pathologically one, interrupted by death, and thus encountered at different stages, was swaying, irresistibly swaying, in an opposite direction.

Beer, in his work on the connective tissue of the human kidney, published in 1859, was calling attention to two distinct forms of interstitial hyperplasia, which he had observed in renal disease: the one circumglomerular, the other intertubular. The circumglomerular interstitial nephritis was, according to him, marked clinically by yellow-coloured urine, of low specific gravity, and presenting little urinary sediment; whereas the intertubular commenced with hæmaturia, and was attended by urine of high specific gravity, and possessing much sediment.

Traube writes in 1860 (*Klinische Untersuchungen*, page 969), appealing that the name of Bright's disease should be given up, because it promulgated error, and led to the confusion together under one head of a great variety of forms of renal degeneration; the parenchymatous inflammation did not constitute it; this was a first change only, which might lead to it. Interstitial nephritis, or interstitial hyperplasia, could be developed without any previous stage of parenchymatous swelling; and parenchymatous swelling was to be found in the renal changes secondary to old heart-affections. Typical parenchymatous swelling existed in the kidney of variola, and in all other acute febrile processes; but this did not necessarily go on to degenerative renal disease. At the same time, he admitted that glandular or parenchymatous swelling of the epithelium of the cortical tubes was an ordinary accompaniment of interstitial nephritis, and of amyloid disease of the vessels of the kidney.

Acts of Parliament and the Queen's pleasure apart, there are few things so difficult to shake yourself quit of as the name of a place, or of a man, or of a disease. While Traube was urging that the name of Bright's disease should be surrendered, because of its vagueness and uncertain applicability, Dr. Goodfellow, in some admirable Lectures on Diseases of the Kidney, published in 1861, was as strongly recommending its re-adoption in England, in lieu of albuminuria, for a varied but peculiar (specific) renal degeneration, which possessed certain well ascertained symptoms, and a moderately precise pathology of its own. He writes (p. 237): "It is from not separating the acute from the chronic stages, and from taking the mixed varieties as so many independent forms, that so much confusion has arisen."

Goodfellow was no blind believer in casts; he advised those who wished to make a sound diagnosis of the extent, and would forecast the issue of any case of renal disease, to go back to estimating the amount of urea excreted *per diem* by the patient; and directed attention to the grave secondary danger undergone by the blood, when the normal elimination of urea was rendered defective, in consequence of any renal inadequacy.

Dr. Goodfellow's lectures showed considerable knowledge of foreign labours, as well as original ideas. He argued (page 54), that the impurity of the blood in chronic renal disease might act, much as solutions of urea in laboratory experiments, in destroying the red blood-cells, and causing them to break up. At page 217, he compiled a valuable table of measurements of the tubuli uriniferi, and of the small arteries of the kidney; and he was the first, at all events in this country, to recognise the important part played by the arteriolæ rectæ as channels whereby the blood could pass from the renal artery by a short

cut into the renal veins, when the circulation by the longer route through the Malpighian bodies in the cortical substance, was obstructed by swelling of the tubules, or effusion of fibro-serum into the intertubular lymphatics—a point which had been insisted upon by Professor Virchow in a very interesting pamphlet, published about 1860.

THE CROONIAN LECTURES ON THE INFLUENCE OF THE CIRCULATION UPON THE NERVOUS SYSTEM.

Delivered before the Royal College of Physicians.

By WALTER MOXON, M.D., F.R.C.P.,
Physician to Guy's Hospital.

LECTURE II.—PART I.

IN my last lecture, I endeavoured to describe means whereby the entry and exit of blood to and from the interior of the cranium are so arranged as to favour the maintenance of a constantly sufficient supply to the brain, whilst obviating ill results of undue stress of blood; and I then passed on to the effects produced when great atmospheric pressure forces blood into the closed cavities which contain the nervous centres; and I finally digressed to point out the weakness in the circulation of the lowest part of the spinal cord, which arises through its more precarious supply from above, and want of reinforcement from below. Whilst upon the arterial supply to the spinal cord, it occurs to me to observe a point which has struck me forcibly in reading descriptions of experiments made for the purpose of tracing the course of fibres in the cord, because the mode in which the arterial supply may influence the results of such experiments seems apt to escape notice; and this may be a part of the reason why different observers differ in their results. Thus, for instance, in one of the experiments made by a great master in this branch of investigation, a comparison is set up between the effects upon the sensibility of posterior nerve-roots when incisions are made near together across the posterior columns above and below a single pair of roots, and the effects produced when similar incisions are made far apart, including five posterior roots between them. When such incisions are close together, sensation in the single pair of roots between is lost; when the incisions are far apart, the roots not only retain their sensibility, but appear rather more sensitive than natural. If we bear in mind the posterior spinal arteries and the mode of their reinforcement by occasional branches on the nerves, we shall see that, when the incisions are close together, the posterior spinal arteries above and below are severed, and the small segment is drained of its blood, so that surely insensibility would arise from this cause alone. If, on the other hand, the incisions include as many as five nerve-roots between them, there is a very great probability indeed that a large reinforcing artery will enter the posterior spinal in so great a length, and thus maintain a blood-supply. But it may be asked, Will such an explanation serve to show why the sensibility is increased? We must not, however, assume that evidence of unnatural tenderness is a proof of increased sensibility; this, no doubt, is not the case. I have now under my care in Philip ward a man who has paralysis and insensibility to touch in his right leg, but nothing the matter with his left leg. In this man, a pinch which causes only a smile when applied to his sound limb, produces a cry and a request against its repetition when it is applied to the limb which cannot feel a touch or localise the pinch. Hence signs of pain do not prove sense of touch, and the conductors of normal sensibility cannot be traced by signs of pain. In this man, the skin of the affected limb is pinker and thicker than the skin of the sound limb. This far from unprecedented case shows that we may expect proofs of unnatural sensitiveness to coincide with considerable anæsthesia; and the unnatural sensibility to pain in the posterior roots may itself be taken as some evidence that the normal sensibilities of the part were reduced. In following out the points that have arisen with reference to the circulation of the spinal cord, I have digressed considerably from the main line of my argument, which is bent on inquiring into the soundness of the view which teaches that congestion of the brain is an essential or primary disease.

And now I will return to the effects of caisson-pressure upon the brain, if one can so speak, when we find that the pressure had no effect