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ON THE

DIAGNOSTIC VALUE

OF THE

CORPUSCULAR BLOOD-ELEMENTS IN THE URINE

OF

BRIGHT'S DISEASE.

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Most general practitioners of medicine, when called upon to investigate an obscure case of Bright's Disease, have probably felt the want of some more definite guides to the exact condition of the kidneys than those furnished by the proportion of albumen in the renal secretion, or the character of the tube casts which the urine contains; and although it seems at first sight an arduous task to attempt supplying the student with any additional aid beyond that afforded by the admirable manuals published by Doctor Dickinson, and, more recently, by Doctor Grainger Stewart, yet my connection with the hospital has enabled me to carry on some researches which, enlightened by the new discoveries in regard to pus and mucus, may serve to render certain doubtful cases of this affection somewhat clearer than they would be without such assistance. It seems remarkable, indeed, how meagre are the references to the diagnostic importance of blood in the urine made in the monographs above mentioned; the former of these gentlemen observing in respect to casts (p. 18): "If pus [white blood] cells are included, the inflammatory or catarrhal state has taken such hold of the tubes that the epithelial cells are replaced by pus globules. Blood globules will show that there has existed enough congestion to rupture the Malpighian capillaries." While the latter dismisses the subject with little more than the statement (p. 15): "And, lastly, some [casts] are found in which blood corpuscles in varying quantity are present. Along with the tube-casts, and sometimes in large quantity, blood corpuscles altered by the action of the fluid in which they lay [*sic*], are found."

As, however, the important advance in pathological science, to which I have alluded, is still spoken of in this country under the title of "Cohnheim's alleged Discovery," it may not be unnecessary to advert briefly to its merits and the testimony which supports it. Dr. Cohnheim, as the readers of this Journal are aware (see number of this Journal for Oct. 1869, pp. 549–552) first published his theory of Inflammation, and detailed the original and ingenious experiments from which it was built up, in a leading article in *Virchow's Archives* for September, 1867, which soon attracted everywhere the notice of histologists. According to Cohnheim the process of pyogenesis consists first, in a partial interruption of the flow of blood by which the red corpuscles move more slowly through, or almost block up, the capillaries, while white globules adhering to the parietes of the vessels arrange themselves in a layer upon this inner surface of the walls; and second, in the "wandering out" of these white blood cells through the stomata, demonstrated by Recklinghausen in the walls of the finer bloodvessels by virtue of that amœboid movement which is one of the most remarkable attributes of the white blood corpuscle, and so aptly illustrated by an English commentator on Prof. Huxley's lecture upon Protoplasm, when he explains the process of an amœba taking a minute diatome into its substance for food, by comparing it to a lump of dough growing of itself gradually around an apple to make an apple-dumpling: the white blood corpuscles which have thus wandered out then constitute with exuded serum that yellow fluid, so long known under the name of pus, and hitherto generally supposed to be a product of the breaking down of tissue. In support of this doctrine experiments upon frogs and rabbits paralyzed by woorara are described in which the mesentery of the animal being exposed and spread out upon the field of the microscope, multitudes of white corpuscles were *seen* in all stages of transit from the interior to the exterior of the vascular walls, in which latter position they constituted ordinary pus globules.

Of course such a novelty in medical science has met with numerous assailants, among whom the most prominent seems to be Prof. Kolman Balogh, of Pesth, who, in an article in *Virchow's Archives*, (Erstes Heft, Band xlv. S. 19, u. s. w.), asserts that in spite of the most prolonged and careful attention not once could he see the transit of the white blood cells through the stomata in the vascular walls, which he thinks if they exist are such minute pores that they can give passage only to fluids. His observations are, however, sharply commented upon by Dr. A. Schklarewski, of Moskow, in the following volume of the *Archives* (Band xlvi., Hft. 1, S. 116) and Cohnheim's experiments appear (*Transactions of Pathological Society of London*, vol. xix. p. 467) to have been repeated before the London Pathological Society in April, 1868, by Dr. H. Charlton Bastian, of London, with entire success. In our own country Lieut. Col. J. J. Woodward, Surgeon U. S. A., stated during a lecture at the Philadelphia

College of Physicians, May 31st, 1869, that the experiments of Cohnheim had been tested under his direction in the Surgeon-General's Office at Washington, and that he had found the description of phenomena singularly accurate; the observations on frogs being fully corroborated, as far as they had time to repeat them, in every particular, and Dr. William F. Norris, of this city, but for some years past residing in Germany, in an article now in press, detailing observations made, chiefly on the cornea of frogs, in conjunction with Prof. Stricker, of Vienna, while maintaining that some of the corpuscles of pus originate in the proper cells of the tissue, admits as indubitable, that many are in reality white blood globules which have made their way through the walls of the vessels, as Cohnheim describes.

It has been urged, however, by some assailants of this doctrine, that even admitting, for the sake of the argument, Cohnheim's views on inflammation to be correct as regards the inferior animals, upon which his experiments were tried, there is no proof that the same ignoble process of suppuration affects man, a creature of such far higher attributes; but, on this point I trust that my own experiments, published in the *Pennsylvania Hospital Reports* for 1869, will be found conclusive. By diluting a drop of my own blood upon a slide, with pure water introduced at the margin of the thin glass cover, and thus reducing the liquor sanguinis to the specific gravity of the saliva, I found it quite possible to watch every step of the change, in which by mere distension the white blood cell is converted into the salivary corpuscle, with its one, two, or three nuclei, its actively revolving molecules confined by a cell wall of exceeding tenuity, capable of presenting all the phenomena of deep-staining of the nuclei with the entire cessation of movement on the addition of aniline dye. In like manner, when the liquor muci and liquor puris are similarly diluted their corpuscles are also seen for the most part to be converted into salivary globules, and I infer therefore that we may regard the strong presumption afforded by Cohnheim's experiments upon the rabbit as established into a fact, and conclude that most (at any rate) of the corpuscles of *human* pus are simply white blood cells which have wandered out through the vascular walls.

But interesting as these researches are from a scientific point of view, it is only as they can be applied to diseased states of the human organism that they become of real importance to the physician; and my object in the present paper is to make some practical deductions in regard to the congestive and inflammatory processes undergone by the kidneys during the course of Bright's disease. I find, however, that some of the experiments I had planned in relation to this subject have been anticipated by Prof. Axel Key, of Christiania, Sweden, who, in a paper partly translated for the columns of the *Medical Times and Gazette* for May 22d, 1869, p. 542, "On the Behaviour of the White Blood Cells in Inflammation of the

Kidneys and Lungs," informs us that by setting up inflammation of different grades in the kidneys, and at the same time throwing cinnabar injections into the blood, he was enabled to follow the white blood cells in these processes; he believes that even in slight irritation the white blood cells, without interstitial changes and without hemorrhage, escape from the vessels into the renal glomeruli, and force their way into the tubes, sometimes one by one, and sometimes several together, and are found in the urine under the appearance of pus cells. Unlike Cohnheim, he thinks it is an absurdity to consider the white blood cells as pus corpuscles under all circumstances as soon as they have left the walls of the vessels, and is of the opinion that he has found that the leucocytes may remain on the lining membrane of the tubules, and develop into epithelium. He further states: "In morbid changes in the kidneys, the cells which have migrated from the glomeruli and from the interstices into the tubes, and which resemble pus cells, may occur in great abundance in the urine, both isolated and forming whole cylinders, without the slightest trace of suppuration or actual pus formation being discoverable in the kidneys." These views in regard to the significance of pus (white blood) casts, contradictory as they are, not only to the opinions of older authorities on Bright's disease, for example George Johnson (*Diseases of the Kidney*, p. 418), but also to those of recent writers, such as Beale, Dickinson, and Grainger Stewart, nevertheless fully coincide with my own clinical observations as will be seen in the sequel. It will perhaps be objected as before, however, that since they were made upon inferior animals alone, they afford no proof that the same changes occur in man, yet this doubt can be easily set at rest by a simple modification of my experiments, such as diluting specimens of fresh human urine containing pus or mucous globules, until a hydrometer immersed in the fluid marks the specific gravity of 1005, when on examination with a sufficiently high power the ordinary salivary corpuscular form of the white blood cell may be readily detected.

If now, aided by these various researches, we endeavour to trace the course of renal inflammation in its simplest form, that from traumatic irritation, we are led to conclude that a first departure from a state of perfect health may originate in the mere mechanical effect, through pressure, of some foreign body, such as a small uric acid calculus, or a plug of adherent white blood corpuscles, acting exactly like the hot iron or filament of thread used by Cohnheim to set up inflammation in the cornea of the frog. This produces a partial or complete stasis of the blood in the neighbouring vessels, whose first or least amount results in the migration of a few leucocytes and the exudation of liquor sanguinis, which, mingling with the urine, renders that fluid slightly albuminous; the second or medium degree in the formation of tube casts called fibrinous (sometimes it appears to me on insufficient evidence), and the abundant "wandering out" of the white (accompanied by a few red) blood cells through

their power of amœboid movement, as described by Cohnheim, and well known to occur in inflammation of mucous membranes analogous to that lining the uriniferous tubules; lastly, when of its third or highest intensity, in the free escape of the red blood disks in addition to the other elements alluded to, either *per rhexin* or by their peculiar mode of exudation through the walls of the minute capillaries.

As examples of the first of these forms occurring in other tissues of the human organism, may be instanced the anasarca produced by an abdominal tumour obstructing the reflux of blood through the vena cava, the œdema of the eyelids in the forming stage of hordeolum, and the flow of transparent serous fluid during the early period of an ordinary cold in the head.[1] The second is illustrated by the secretion of pus in acute cystitis, or its development in an ordinary phlegmon ; and the third finds its analogue in the mingled pus and blood discharged from the mucous membranes during the height of an attack of gonorrhœa and rarely of virulent ophthalmia. Of course, like the inflammatory process in other portions of the system, nephritis may terminate naturally by resolution, or be cut short by successful treatment in either the first or second stage, as above described ; a restoration of the affected parts to perfect health, doubtless so terminating as a rule in the gradual retrograde manner, we daily observe in convalescence from an attack of inflammation of the conjunctiva or of the Schneiderian membranes. It would seem, however, that white blood corpuscles imbedded in delicate hyaline casts, as well as floating freely in the urine, may rarely continue to occur for some time after the ordinary symptoms of Bright's disease disappear, being perhaps merely the results of previous inflammation from time to time washed out of the uriniferous tubules, as probably took place in Case VI., below detailed. It must by no means be supposed that I mean to assert the process of inflammation in the living organism presents such sharply-defined stages as those above described ; on the contrary, just as a naturalist is perplexed when called upon to draw the dividing line between the animal and vegetable kingdoms, so the morbid anatomist, and *à fortiori* the physician, will occasionally meet with cases of nephritis, where it is almost impossible to decide the grade of inflammatory action. It would appear, however, that such examples are exceptional, and that in a large majority of instances the unhealthy condition can be classed in one of the three categories just mentioned. Indeed, on seeking to arrange the collection of facts I have gradually accumulated in regard to Bright's disease during

[1] Dr. Dickinson quotes (*Pathology and Treatment of Albuminuria*, p. 15), Dr. George Robinson of London, as having proved experimentally on animals that albuminuria resulted from ligature of the renal vein, and Dr. Grainger Stewart (*Bright's Disease of the Kidneys*, p. 33) has confirmed this statement by his own observations.

numerous examinations of specimens from patients in the hospital wards, and also in the private practice of medical friends, as well as in my own, I find most series of phenomena are capable of being grouped together in accordance with the views above expressed, and serve to elucidate one among the many important applications of which the doctrines of Cohnheim are susceptible.

In order, however, to determine from microscopic examination of the urine, not only the grade of inflammation, but its tendency (*i. e.*, whether advancing or retrogressive), several observations upon specimens obtained at intervals of a day or two will generally be necessary, and that they may afford the greatest assistance in diagnosis, these should be made comparative in their character. The method I have been led to adopt for the accomplishment of this object has at least one merit, that of simplicity, as will be seen by the following description: The sample of urine to be tested is placed in a conical graduated measure of at least four fluidounces capacity, carefully covered and allowed to remain undisturbed for twelve hours, when the bulk of deposit is noted; a small amount of the sediment is removed from the bottom of the vessel by means of a glass tube drawn off to a moderately fine point, two or three of the last few drops that have entered allowed to escape and the outside of the pipette wiped dry; a minute portion of the remaining contents is then deposited upon a slide, covered with a square of thin glass measuring exactly half an inch across, and the surplus moisture absorbed from the margin of the covering glass by a soft linen rag, great care being taken to avoid movement of or pressure upon the square It is obvious that by adjusting a slide thus prepared upon the stage of the microscope, so that for instance the right upper corner of the cover shall occupy the field of view, and by means of the horizontal stage movement running it across until the left upper corner appears, then raising the stage with the vertical movement the width of a single field, reversing the horizontal motion as far as the right border, and so on, every part of this film of fluid measuring one-fourth of one square inch may be examined and the number of its contained red and white corpuscles, tube casts, epithelial cells, &c. accurately ascertained. The apparent magnitude of this surface when viewed under a one-fourth inch objective giving an amplification of two hundred diameters will, of course, be nearly seventy square feet, so that time would be needlessly wasted in enumerating all the cells, &c. seen in such an area, except when very sparsely distributed; if abundant, counting those seen in a few fields, or even in sundry thousandths of an inch (as marked off between the threads of the cobweb micrometer), and noting the average, will often answer every purpose. Although for estimations of this kind a quarter of an inch objective is amply sufficient, I have constantly found great advantage from a subsequent examination with a very high power, afforded by an objective of much shorter focus, for while by deeper eye-pieceing an equal enlargement

may be obtained, yet obscure points of structure can be much better seen *for the first time* by the aid of a twenty-fifth, for example, magnifying twelve hundred diameters with the lowest eye-piece, than with a quarter or eighth so combined with powerful eye-pieces as to yield a similar amplification ; such at least is the result of my experience in hundreds of trials, and I feel confident that additional benefit will often be derived from the use of a fiftieth, which I have just procured from Messrs. Powell & Lealand, as, for instance, in the diagnosis of white blood corpuscles from the nuclei of renal epithelium, and in the detection of those very minute oil globules which mark the earliest stage of fatty degeneration in the cells of the uriniferous tubules.

Since any consideration of the diagnostic values possessed by other constituents of the urine in Bright's disease does not fall within the scope of my present paper, as stated above, I propose to dismiss the forms of albuminuria in which the chief or important lesions are fatty, amyloid or granular degeneration, and confine myself to the consideration of those pathological states where red and white blood cells appear in the urine, and can be regarded as indicative of some renal affection. It is obvious that vesical or urethral irritation may at any time cause the urine to exhibit most of the chemical reactions and microscopic appearances found in Bright's disease, and cases doubtless occur in which it is impossible to distinguish at a first sight whether the blood elements are effused in the bladder or kidney, yet by a careful investigation, not only of the local and general symptoms, but also of the history of the patient, correct conclusions may generally be obtained. In the following instance it seemed, however, impossible to determine the seat of the malady until a second examination disclosed the existence of tube casts:—

Case I.—Mr. J. L., æt. 50, consulted his family physician on the 26th of September, 1869, on account of the condition of his urine, as he supposed he was passing blood. Careful investigation failed to reveal any constitutional or local symptoms of disease except slight pain in the loins, a little uneasiness in passing water, and some diminution in the amount of fluid voided during twenty-four hours ; no exciting cause of the seizure could be discovered, nor was there present any diathesis hereditary or acquired which might be considered as a predisposing agent. Four fluid-ounces of his urine passed the next morning were of a bright red colour, and on standing let fall a dense pinkish deposit which occupied about f℥iij of the liquid ; under the microscope this sediment was found to be composed chiefly of red and white corpuscles in the estimated proportion of fifty of the former to one of the latter : there were also numerous epithelial cells chiefly vesical, many of which were deeply stained with hæmatin. A specimen of next day's urine, after he had been cupped on the loins, was much lighter in colour, and on microscopic examination was found to deposit but about one-twentieth the amount of corpuscular blood elements existing in the water passed the day previous, although the coagulum produced by heat and nitric acid was at least one-fourth as bulky ; thus indicating that the albumen did not proceed solely from effused blood.

The sediment also contained a large amount of oxalate of lime, and on examining the fourth of a square inch of urinous film one well-marked cast inclosing white blood cells and several doubtful aggregations of matter resembling tube casts were discovered. A specimen of the urine brought to me on the 22d of October was found to be normal in colour and appearance, specific gravity 1020, neutral in reaction, and when tested with heat and nitric acid still showed a notable amount of albumen, the coagulum not exceeding, however, one-twelfth of the fluid boiled. Three ounces allowed to stand undisturbed in a conical glass deposited nearly f℥ij of light cloud-like sediment, which under the microscope showed a very few oxalate of lime crystals, about on an average twenty blood corpuscles, of which four were white globules, to each field, and in one-fourth of a square inch of urinous film two well-marked faintly granular casts. At the date of this last examination the patient showed no obvious symptom of disease, and reported that he had enjoyed fair health through the interval and passed no more blood.

Among the means of distinguishing when the effused blood is of vesical and when of renal origin, it is to be noticed that the seat of pain or soreness on pressure is one of the most important; of less general application, although of course more positive when it occurs, is the existence of tube casts in the urine, which, when indubitable, prove, I believe, that we have to deal with nephritis. Care must, however, be taken to avoid confounding accidental aggregations of matter with genuine casts from the uriniferous tubules, for I have seen at least a thousand pseudocasts, and excellent imitations too, that were produced in an instant by a slight sliding movement of the thin glass cover. It is not, I believe, common to meet with more than two or three specimens of the rounded epithelium from the uriniferous tubules upon a single slide, unless desquamative nephritis exists, and should the cells exhibit distinct oil globules, even although not more than $\frac{1}{3000}$ of an inch in diameter, great force would be added to the presumption of Bright's disease, derived from the presence of the blood elements associated with renal epithelium. It is also, I think, rare for us to detect the amœboid movement, and unusual to find even the irregular shape which precedes the complete death of the motionless leucocyte in pus (white blood) corpuscles from the kidney, while this motion may often be observed in the urine of cystitis, especially if examined while fresh and without being allowed to cool below the normal temperature of the body. As mentioned by Prof. Beale, phosphatic crystals seldom occur with pus-cells from the kidney, a useful aid to diagnosis when we are able to exclude suspicion of coexisting trouble about the bladder. Of course the detection of tube-casts with red and white corpuscles imbedded in their substance is a positive index of Bright's disease.

Supposing now that by the assistance of any or all of these indications we have been able to eliminate vesical irritation as a cause of the presence of blood-elements in the urine, it remains to be seen how far the actual

number and relative proportion of the red and white corpuscles serve to point out the past, present, and future of the renal affection.

First. When the red blood globules very largely exceed the white in number, approximating to the proportion in normal blood, it is probable, as intimated above, that rupture of some small vessels has taken place, and the flow of blood is a true hemorrhage from the kidney, which may be produced by blows across the loins or lacerations caused by angular calculi. This opinion will be further strengthened if a thorough search fails to reveal any tube-casts, and if the albumen as coagulated by heat and nitric acid is no more than should exist in an amount of liquor sanguinis corresponding to the bulk of deposit formed of cell walls from the red disks.[1] As an approximative guide for determining this last point, I find by experiment that a fluidrachm of blood stirred up in two fluid-ounces of water lets fall, on standing twelve hours, a whitish deposit of fibrin and cell-walls, measuring about two fluidrachms, and that a portion of the supernatant liquid tested with heat and nitric acid yields a coagulum, chiefly albuminous, occupying about one-fourth of its bulk.

In the following example the irritation appears to have been mechanical, but no evidence of resulting nephritis could be detected.

Case II.—E. R., gentleman, æt. 60, consulted his medical adviser in the early part of June, 1869, on account of a dull pain in the region of the right kidney; he had also been troubled with a little dyspepsia and a slight tendency to diarrhœa, but had not been exposed to cold, or suffered any strain or blow in the dorsal region. There was no pain in the bladder, no history of gravel, and no perceptible gouty diathesis, although his father had been the subject of some renal irritation in advanced life. He had no headache, no œdema of the face or ankles, and the very faint febrile movement seemed obviously due, with the slight diarrhœa, to a little gastro-intestinal catarrh. The urine, which was quite dark in colour, was found to be acid; specific gravity 1021; free from sugar but yielding a slight cloud on the application of heat, which, as it did not wholly disappear after nitric acid was added, doubtless indicated the presence of albumen. On placing a drop of the urine from the bottom of the glass beneath a microscope, the deposit was found to consist of small crystals of oxalate of lime, and red and white corpuscles, the former generally quite decolourized. As the blood-elements bore to each other almost their normal proportions, it seemed probable that they proceeded from some abrasions or other solutions of continuity caused by small angular renal calculi rather than from an exudation through the walls of the vessels, an opinion almost substantiated by the subsequent history of the patient, who rapidly convalesced under suitable treatment for the oxaluria, and when last heard from, four months later, was in excellent health.

Second. When in Bright's disease the white blood corpuscles are mingled with red disks in a proportion exceeding one twenty-fifth of the latter, my observations lead me to conclude that generally the patient is suffering

[1] See my paper in the Am. Journal of the Med. Sciences, July, 1869, p. 53.

from an acute or subacute inflammation of one or both kidneys, and attended with danger therefrom more or less serious, according as the amount of corpuscular elements shows by its absolute quantity that a larger or smaller portion of the kidney is inflamed. If the albuminous coagulum produced by heat and nitric acid occupies more than one-half the fluid tested, and many times exceeds that which would be furnished by the liquor sanguinis corresponding to the blood corpuscles, an extensive inflammatory disease probably exists, unless careful microscopic scrutiny shows decided fatty degeneration (and consequent loss of secretive power) in the epithelium of the uriniferous tubules. The following case, for whose complete history I am indebted to the note-book of my friend George Pepper, M. D., illustrates some of the views above enunciated.

Case III.—G. M., wheelwright, æt. 43, married, and father of four healthy children, was admitted into the men's medical ward of the Pennsylvania Hospital, 12th August, 1869, under the care of Dr. J. Forsythe Meigs, to whose courtesy I owe permission to make use of this report. The patient stated that he came of a long-lived family, and had always enjoyed good health; that he had been in America about eleven months, and had a stormy passage out, during which he was somewhat exposed. His habits have been moderately temperate, and he has never had any venereal disease. Fifteen years ago he injured his hand, losing the third and little fingers, but the wound was carefully treated, healing up within thirty days, and without extensive suppuration. For several years past he has always been obliged to rise once or twice during the night to urinate, but the water has never been smoky or bloody; during this period he has noticed a slight puffiness of the ankles after long walks or prolonged standing. About two months before admission his feet first began to swell, at which time he appeared to be in his usual health, and had no new symptoms, but soon after he had an attack of profuse diarrhœa, unaccompanied by backache, pain in the bladder, enlargement of the abdomen, or puffiness of the eyelids, and not severe enough to confine him to bed, even for a day, or prevent him from working as usual. From that time the dropsy gradually increased, invading the legs, thighs, scrotum, and abdomen, until about two weeks before his entrance into the hospital, the skin of his legs cracked open in several places, and a profuse discharge of serum occurred. On admission, his complexion was pale and waxy; his legs were enormously swollen (the calf measuring $18\frac{3}{4}$ inches in circumference), fissured, and the skin covered with chronic eczema; a slight squamous eruption, bran-like in appearance, also affected the face, neck, and upper portion of the thorax. There were no abnormal heart sounds, cough, or dyspnœa; bowels rather loose, although at times regular; appetite good, and tongue clean but pale. He passed water frequently and in great abundance, which, on examination by the resident physician, was found to be light coloured, slightly acid in reaction, and on being tested with heat and nitric acid, to yield about one-eighth of its bulk of albuminous coagulum. On the 16th of August, when his general condition was much the same, although the swelling of his legs had diminished, and the eczema had disappeared, he passed seventy ounces of light-coloured urine, of the specific gravity of 1018, and still containing a large amount of albumen. Of this urine I obtained a specimen for the first time, and on examining

the rather abundant deposit which it let fall, I found it to be composed of white and red blood corpuscles, in proportion of one to five, a few darkly granular, faintly granular, and pale hyaline casts, and numerous elongated masses, composed chiefly of epithelial cells, which appeared to have undergone a remarkably equal fatty degeneration. These latter casts did not soon become tinted with aniline, as ordinary fibrinous and hyaline casts, although not germinal matter, readily do. On the 1st of October his condition was decidedly improved; he had gained flesh and colour, had a good appetite, and slept soundly at night. He had then no dropsy, but the urine continued abundant, amounting to eighty fluidounces in twenty-four hours, and still obliging him to rise in the night to micturate at least once and sometimes twice; heat and nitric acid continued to throw down a bulky coagulum of albumen. On the 15th of October a specimen of urine, of which he passed ninety-six ounces in a day and night, was examined carefully as above described, when it was found that one-fourth of a square inch of urinous film from the three fluidrachms of light cloudy deposit let fall by four fluidounces standing twelve hours, contained twenty-eight pale granular casts, some inclosing epithelial cells, white blood corpuscles, and red disks; one of these casts, about $\frac{1}{40}$ of an inch long and $\frac{1}{800}$ of an inch in diameter, faintly granular in character, had imbedded in it two white blood corpuscles, five red ditto, and one epithelial cell. Numerous red and white blood globules floated freely on the slide, in the proportion of about one white to twelve red, the latter averaging five to each field. Under a power of 1200, the generally hyaline casts were seen to have small particles of granular matter resembling oil globules deposited upon their surfaces. The epithelial cells were only slightly fatty, the particles of oil not exceeding $\frac{1}{25000}$ of an inch in diameter. By the careful addition of aniline dye at the margin of the cover the large single nucleus of each epithelial cell, the one, two, or three nuclei of the white blood corpuscles, and the delicate membranous (or membranoid) wall of the red blood disks were brought out in a distinct and beautiful manner, dissipating in this instance, all difficulty in diagnosticating, each from the other. The coagulum produced in this urine by the application of heat and nitric acid, and also by heat alone, was still quite abundant, occupying fully one-fourth of the fluid tested; but in spite of this constant drain upon his system, the patient, under the influence of judicious treatment, nutritious food, and the excellent sanitary condition of the hospital, continued to gain flesh and strength, and on the 22d of October had wonderfully improved in general appearance.

Case IV.—Exemplifies that frequent occurrence in the course of Bright's disease, an acute attack supervening upon one of the chronic forms, as follows:—

Ellen G., cloak-maker, æt. 29, unmarried, was admitted into the Women's Medical Ward of the Pennsylvania Hospital, May 2d, 1869, during the service of Prof. J. Aitken Meigs, who has kindly permitted me to report the case. The patient stated that her father died of consumption twenty-six years before, and her brother of dropsy in his twenty-second year. She had worked very hard at her trade for the last ten years, sometimes as much as fifteen hours daily, and during that time, nearly eight years since, had a severe attack of yellow fever, subsequent to which she had suffered much from dyspepsia, and been troubled occasionally with eruptions upon the face. About five weeks before admission she

took a very severe cold, after exposure to wet, which was followed by a sense of weakness in the loins that gradually developed into a sharp pain in the lumbar and abdominal regions; nausea and vomiting, loss of appetite and intense thirst came on about the same time. One week later she first noticed puffiness of the eyelids; and a few days afterwards enlargement of the abdomen and œdema of the feet and legs came on. Shortly after taking cold she noticed that she was obliged to rise three or four times in the night to pass water, also that the fluid when voided was dusky, and deposited, on standing, a sediment that looked like coffee grounds. For the week following her exposure she had a troublesome diarrhœa, but since then her bowels have been regular, although severe griping pains in the abdomen still persisted. Throughout the week previous to admission she had been troubled with roaring noises in her head, but she did not suffer much from headache, and her intellect was quite clear. On entering the hospital her face, feet, limbs, and abdomen were all very œdematous, and her countenance presented the pale, waxy hue of Bright's disease in a very marked degree. A specimen of her urine examined on the 24th of May was of a dark reddish-brown colour, specific gravity 1010, and contained about one-third of its bulk of albumen as coagulated by heat and nitric acid. Under the microscope I found the abundant deposit let fall on standing was composed of large numbers of red and white blood corpuscles in the estimated proportion of twenty-five to one, much granular debris, and some well-defined casts, granular, fatty and fibrinous, all more or less stained with the hematin from the decolourized red globules; some of the tube casts had imbedded in their substance epithelial cells which had undergone marked fatty degeneration, many of the oil globules measuring $\frac{1}{10000}$ of an inch in diameter. Under the influence of appropriate saline diuretics the flow of urine rapidly increased, and five days after the above examination was made the amount passed in the preceding twenty-four hours measured 112 fluidounces, which free diuresis soon produced a very satisfactory decrease in the anasarca and ascites, but I was unfortunately prevented by illness from making further examination of this patient, and can only add that she was discharged from the hospital on the 7th of August very much relieved.

The next instance is one in which the slight local nephritis of short duration appeared to be traumatic.

Case V.—N. C. D., merchant, while apparently in usual good health, was attacked suddenly after breakfast on the 20th of September, 1869, with intense pain in the region of the left kidney, extending downward toward the groin. A specimen of his urine, examined on the 26th, was found to contain many uric acid crystals, numerous red and white blood-corpuscles in nearly equal proportions, and in half a square inch of urinous film three casts of the uriniferous tubules, having white blood globules and epithelial cells imbedded in their substance. The amount of albumen appeared to be but little more than that proportionate to the blood corpuscles, so that it was deemed probable that an angular calculus of uric acid had suddenly changed its place in the kidney, become impacted and set up a local nephritis confined to the small portion of renal structure in its immediate neighbourhood. The pain in the loins returned at intervals for some days, gradually becoming less severe, and under alkaline treatment passed off in about two weeks from the first attack, leaving the patient in good health, which he has enjoyed up to the present date (Oct. 22d, 1869).

Lastly, should we discover on examination that the white blood cells (hitherto designated as "mucous corpuscles," "exudation corpuscles," and by Dr. Beale "cells closely resembling pus corpuscles."—*Microscope in Practical Medicine*, p. 219) pass off from the kidneys with little or no admixture of the red disks, we may conclude that a chronic inflammation of the organs exists less or more extensive as the number of the leucocytes is smaller or greater and as the amount of fatty degeneration, estimated as above suggested, is serious or otherwise; for my researches tend to show that the one cause of albumen in the urine varies inversely as the other; that is, if in a given case of Bright's disease the urine containing say one-fourth of its bulk of coagulated albumen after boiling, shows many white blood corpuscles with epithelial cells only slightly fatty; and another specimen of the same, collected perhaps two months afterwards, exhibits with the same amount of albumen few leucocytes but epithelium containing large oil globules, we may conclude that (following Dr. Grainger Stewart in his classification on the basis of Virchow's), we have to deal with the First or Inflammatory form (involving a large portion of the organs), which has passed from stage *a*, that of Inflammation, to stage *b*, that of Fatty Transformation; many cases, however, seem to run a much more favourable course, the pus corpuscles diminishing in number without any corresponding advance towards fatty degeneration in the epithelial lining of the tubules, so that the albumen slowly decreases in quantity, and the patient regains at least a comfortable state of health, as in the following example.

Case VI.—X. Y., merchant, native of Philadelphia, but for some time past residing in one of the New England States, came under my observation August 8th, 1869. From his family medical attendant I learned that about six weeks before he had been exposed to cold and wet, which, acting upon a constitution enfeebled by the poisonous effect of lead and various other causes not necessary to mention here, had resulted in an ill-defined febrile attack, attended with pain in the back, and high-coloured urine; but that unfortunately from the fact of the physician himself being at the time an invalid, no examination of the renal secretion was then made. During the first week in August he was seen in consultation by Prof. Alonzo Clark, of New York, who, on testing the urine, discovered, as I was informed, a notable amount of albumen and several delicate hyaline casts of the uriniferous tubules. My first examination of the morning urine, made during the evening of August 9th, with the precaution above described, showed in three-quarters of a square inch of urinous film twenty-five or thirty epithelial cells, some of which inclosed very minute oil globules, about an equal number of free white corpuscles, and some exceedingly delicate hyaline casts, two of which contained one or more leucocytes; no red blood globules were detected; on testing with heat and nitric acid only a moderate opalescence of the liquid was produced, but this trace was deposited next day into a thin film upon the bottom of the tube, which proved entirely amorphous under the microscope. Frequent examinations of the urine from this patient were made with similar results, except that the amount of albumen gradually decreased until on the 27th

of August my note-book states that the urine was clear and normal in both colour and quantity, and on testing with nitric acid not the slightest cloud was visible, nor was any produced by long boiling of the acidulated liquid. Four fluidounces set aside in a conical glass for two hours let fall a scanty flocculent deposit which, under the microscope, was seen to be composed chiefly of epithelial cells and white blood corpuscles, but also contained a few very delicate hyaline casts. Three-quarters of a square inch of urinous film when carefully examined showed three transparent casts, one of which contained four white blood cells (pus corpuscles). On the 10th of September the urine was found free from all trace of albumen, and in half a square inch of urinous film could only discover two hyaline casts, the longer containing two epithelial cells apparently healthy, and three leucocytes, the shorter no epithelium, and but one white blood corpuscle.[1]

Except during the first two weeks after I began to investigate his case, this patient had no symptom of renal disease, save the constant, although scanty deposit of casts, white blood corpuscles, and epithelial cells let fall every day by the urine, and although suffering from other effects of lead which complicated his case, the kidneys on the 20th of October, when I last heard from him, appeared to have become gradually restored, if not to health, at least to a condition in which they were capable of performing their normal functions.

It is probably in regard to cases such as this that Dr. Beale remarks (*Kidney Diseases and Urinary Deposits*, 1869, p. 344): "Casts containing pus are not common, although some cells agreeing in many characters with the pus globule are not uncommonly present. Of these cells some are no doubt modified cells of renal epithelium, the germinal matter of which is of much larger size than in health, the formed matter of the cell being nearly absent, while others are altered white blood corpuscles (pl. xvii., figs. 93, 94). . . . I have, however, seen many cases in children and adults, where these casts and cells were most abundant, which have been completely recovered." The "altered and growing white blood corpuscles" figured on "pl. xvii." are, I opine, accurate delineations of white blood globules which have become distended by immersion into urine or other fluid of low specific gravity, as described in the early part of this paper, of which it seems to me any one can satisfy himself in a few minutes by simply repeating my experiments.

Recapitulating now the conclusions above reached, it will be seen that while red and white corpuscles occurring as described in the urine, in their normal proportion point to renal hemorrhage, and the same elements when more nearly equal in number indicate an acute or subacute nephritis, the

[1] Although the urine remained clear when boiled, after acidulation with nitric acid it gave a slight cloud with the delicate carbolic acid test of M. Mehu (*Archives Générales de Médecine*, Mars, 1869), but not being as yet familiar with the fallacies, if any, to which conclusions deduced from the action of this reagent are liable, I merely note the fact as it occurred, intending to make some future investigations in regard to its value.

existence of white blood cells (pus, mucous, or exudation corpuscles) *generally* shows a chronic or, at least, less active inflammatory condition of the kidneys: further, that a series of comparative examinations performed with the precautions above-detailed at intervals of a few days affords an important guide to the effect of treatment, and to the progress of the disease; and, therefore, it may be, I think, safely asserted that due regard being paid to the general symptoms and the occurrence of albumen and tube casts in Bright's disease, we can by a careful study of the corpuscular blood elements, as seen in the urine, diagnosticate the form and stage of the renal affection with much more accuracy than it has heretofore been customary to do.