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BRIGHT'S DISEASE.

LECTURES ON

BRIGHT'S DISEASE:

DELIVERED AT THE ROYAL INFIRMARY OF GLASGOW.

BY

D. CAMPBELL BLACK, M.D., L.R.C.S., EDIN.,

AUTHOR OF "OBSERVATIONS ON THERAPEUTICS AND DISEASE," "THE FUNCTIONAL DISEASES OF THE URINARY AND REPRODUCTIVE ORGANS," ETC., ETC.

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PREFACE.

THE following Lectures were delivered at the Royal Infirmary of Glasgow during the author's official connection with that institution. They were afterwards published in *The Medical Press and Circular*. The subjects treated of are regarded in strict conformity with the views enunciated in the author's pamphlet "On Therapeutics and Disease," published in 1870. Of these opinions, at the time, some were considered novel, if not outré. The satisfaction of seeing many of them adopted by leading members of the profession, even without acknowledgment, is here avowed. Prominently among these may be noted the important rôle ascribed to the products of retrograde metamorphosis as morbific agents, and the explanation of the therapeutic effects of alkalies in lithiasis.

Now offered in this form, revised and amplified, the hope is indulged that the lectures may prove acceptable to some of those who heard them with such courteous attention, to others of the class for whom they were intended, and to practitioners whose time and opportunities preclude the study of more elaborate works.

D. C. B.

29 MONTAGUE PLACE,
RUSSELL SQUARE, LONDON, W. C.

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BRIGHT'S DISEASE.

LECTURE I.

INTRODUCTORY OBSERVATIONS—*Functions and Structure of the Kidney*—Human Urine; its Physical Characteristics, and Daily Quantity—Ultimate Composition of the Living Organism—Cells; their Properties—Minute Structure of the Kidney—*Circulation of Blood in the Kidney*—Urea; whence Derived; its Amount in the Renal Artery and the Renal Vein—Mode in which Urine is Secreted—Health of a Part; on what Dependent—Influence of the Nervous System on the Circulation of the Blood—Experiments of Bernard—Section of the Sympathetic; its Immediate Effects, and Analogy with the Influences of Mental Impressions; Effects of Cold upon the Circulation of the Blood—Albumen in the Urine—Law of *Material Correlation.*

GENTLEMEN,—No real advance has ever been made in medical science which did not immediately relate to the great principles of physiology on which we are all agreed. Mere change, of which we have more than a sufficiency, is assuredly not progress. It is alone in the connection referred to that the elucidation of morbid processes will carry conviction to the intelligent mind, and that scientific Medicine can be expected permanently to repose.

Disease is not so much a superadded entity, as an aberration from health; and it is by investigating the

nature of this aberration step by step, and by carefully estimating the value of our therapeutical agents as *modifying* influences thereof, that we can alone hope to elevate the science of therapeutics above the caprice of fashion and the flattering delusions of self-deception.

Apart from these considerations I have no hesitation in saying that the heaping together of incoherent particulars is positively pernicious. For example, men of scientific pretensions take certain particles of *dead* animal matter, place them possibly in four-and-twenty bottles, and watch the influence upon them of four-and-twenty different solutions called antiseptic, and forthwith rush to conclusions regarding the value of the so-called antiseptic Surgery or Medicine of modern times, relatively to the complicated mechanism of the *living* body!

I have no sympathy, then, for *this penchant* after "original investigation," on the one hand; and I have learned to attach little importance to much that is designated "experience" on the other, for I have so often observed that among the so-called cultivators of medical science there is a class of men who discover everything they set out in search of, and whose "experience" is of such a nature that it is *made to* reconcile with any preconceived notion whatever. The value of experience will depend, therefore, on the perceptive powers and reasoning faculty of the observer; and it is most likely to be true the more the alleged occurrences are in harmony with the admitted laws of matter, or conform, as in the case of the human organism, to the physiological laws whereby life is maintained. There is nothing more fatal to the progress of medical science—a progress in my opinion not consistent with its antiquity—than the prominence which is so frequently

accorded to remote or accidental occurrences, compared with the conjunction of morbid processes relatively to the laws which regulate healthy function. If disease be an aberration from health, that which is true of the whole body must be equally true of any portion of it. Hence, the discussion of the diseases of a particular organ presupposes a knowledge of its healthy functions. For the sake, then, of coherency, and of refreshing your memories, I shall preface what I have to submit to your consideration on the subject of Bright's Disease by a brief epitome of the healthy structure and function of the kidney; after which I shall direct your attention to the conditions that induce structural change, the nature of its varieties, and finally, how such departures from health ought to be treated, according to what I regard the true province and aim of therapeutics just adverted to.

Function and Structure of the Kidney.—The functions assigned to the kidney are, the removal of water, nitrogenous salts representing the reduction of protein compounds, and other saline material no longer capable of being utilised in the economy. Of the nitrogenous compounds the following are the most important: urea, uric acid, hippuric acid, xanthine, creatinine, and colouring extractive matters. Besides these, the urine contains salts of potash, sodium, lime, &c. Healthy human urine is a clear amber-coloured transparent fluid, having a decidedly acid reaction, and a peculiar aroma. Its density varies from 1005 to 1030, according to age and other circumstances. The quantity secreted daily has been variously estimated. The mean may be stated at from 40 to 45 ounces.

In ultimate composition the human body is divided into organic and inorganic compounds; and the ultimate molecules of organisation—the atoms of the physiologist—are divisible into nitrogenous, fatty, and

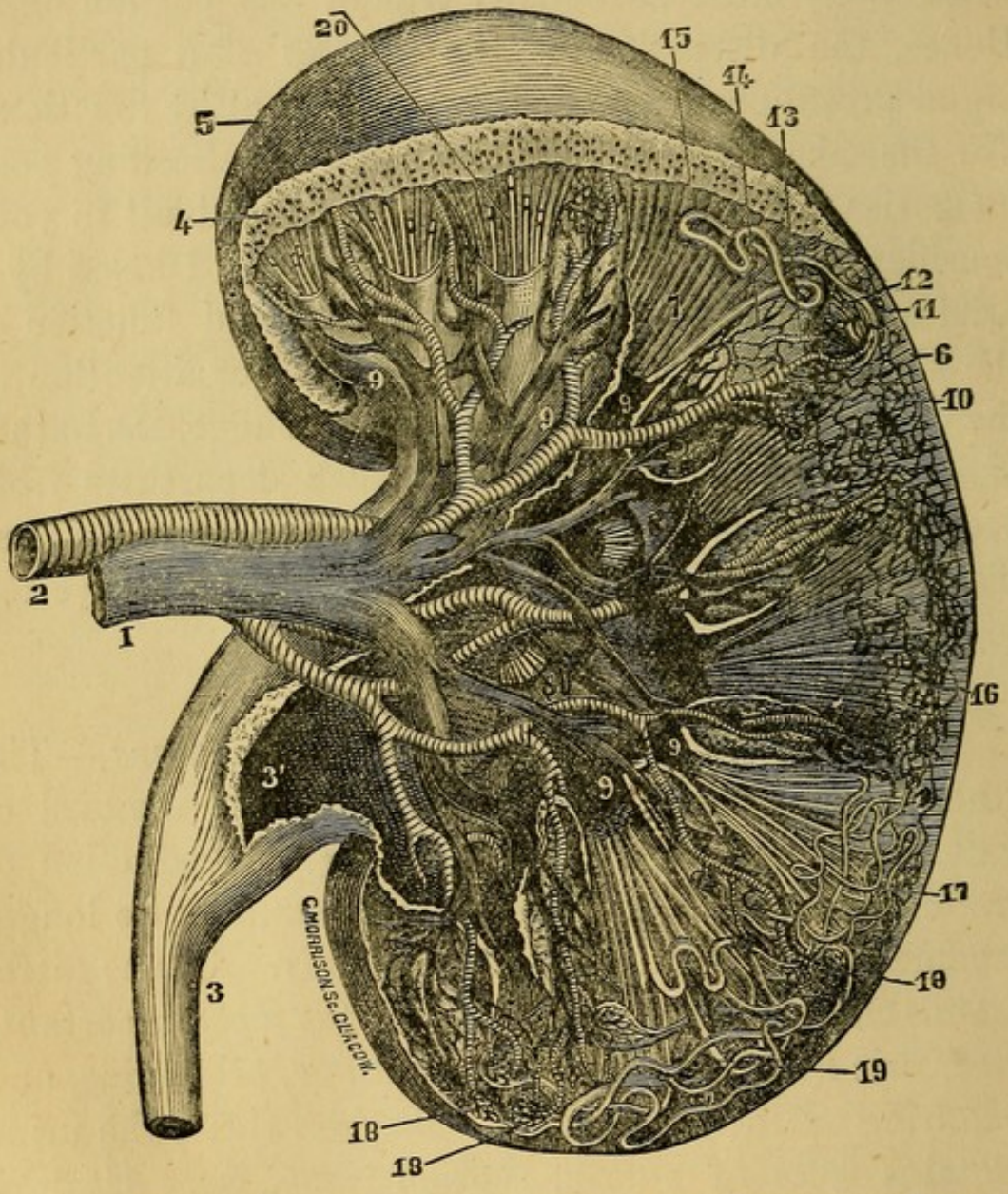

FIG. 1.—GENERAL VIEW OF THE STRUCTURE OF THE KIDNEY—THE TUBES OF HENLE NOT REPRESENTED.—*(After Le Fort.)*

1. Renal vein; 2 Renal artery; 3 Ureter, continuous with the open pelvis; 4 Cut cortex of the kidney; 5 Surface of the kidney; 6 Cortical substance; 7 A Malpighian pyramid with its arteries: 8 8 Papillæ of pyramids which have not been divided; 9 A divided calyx, embracing a pyramid; 10 Branch of the renal artery between two pyramids; 11 Malpighian capsule magnified 40 diameters; 12 Vessels in the centre of the glomerulus; 13 Efferent vessel of the glomerulus; 14 Capillary network; 15 Convoluted tube of the cortical substance × 20; 16 Tortuosities of convoluted tube; 17 Tortuous tubes × 40; 18 18 18 Glomeruli × 10 × 20; 19 Tortuous tubes × 20 to 25; 20 Some tubes cut.

mineral. Growth and secretion consist in an appropriation of these, in the former case for the building up of the body—of compensating for the destruction of tissue—and in the latter for the purpose of elaborating principles which subserve intermediate purposes in the economy prior to their being discharged as excreta. If we suppose a scale of organisation, the one extreme may be regarded as the ultimate molecule; intermediate, the chyle corpuscle; and the other, the fully formed structure of the body, bone, muscle, brain, &c. The active agent in this mysterious process, to whose totality we apply the term life, is the primitive cell. For the building up of the body cells exist in the form of nutritive centres so admirably described by Goodsir; and for the purposes of secretion they are found, as an essential part, in all the secretory and excretory organs. The difference between growth and secretion is simply this: in the former case the cell dissolves in, and with its contents is converted into tissue; in the latter, it dissolves and throws out its contents on a free surface. All secretory surfaces possess this feature in common—viz., cells on a free surface continuous with the exterior of the body, and separated from the blood simply by the interposition of a thin membrane. Cells exhibit these essential properties: (1), vital selection (a term which I employ for want of a better); (2), osmosis; and (3), chemical combination.

If germinal centres receive sufficient healthy pabulum from the blood, healthy repair is effected. If their normal action is exaggerated by too abundant a supply, hypertrophy is the result; if deficient, atrophy. If a secretory organ have presented to it impure blood, depraved secretion is the consequence; and depraved

secretion may in turn occasion structural changes. Again, if the specific gravity of the blood undergo variation from that of health, or if the current of normal blood be interrupted, we find sufficient indications of this state in the various forms of dropsy.

A longitudinal section of the kidney being made, the following morphological peculiarities are observed:—The gland—if, indeed, it can with propriety be called a gland—is seen to be composed of an external or cortical portion, and a medullary. The cortical portion occupies the entire surface of the organ, is of a dark brown, or chesnut colour, and forms a layer of about two lines in thickness. It is friable, easily lacerated, and when this does happen, laceration usually takes place in a direction vertical to the surface. The rupture presents a lacerated appearance, due to an admixture of straight and convoluted tubes, and Malpighian bodies. The straight tubes in the cortical substance are continuous with those in the medullary substance, and are surrounded by convoluted tubes, into which they pass at their sides and outer extremity. (Fig. 1., pp. 12.)

From the cortical substance prolongations are sent inwards towards the pelvis of the kidneys, and between the pyramids termed the *septula renum*, or *columnæ Bertini*. The medullary portion is arranged in the form of cones or pyramids—the pyramids of Malpighi—which vary from twelve to fifteen in number, and these again are composed of uriniferous tubes. This leads us to a consideration of uriniferous canals.

By the *Malpighian capsule* of the kidney is understood a small round body situated at the end of almost every tubule, and giving origin to them. This capsule is surrounded by a membrane called the *capsule of Bow-*

man, continuous with the uriniferous tube. At a point opposite to the entrance of the afferent artery, and the exit of the efferent vessels, the glomerulus opens into and becomes continuous with the canal of the convoluted tube. At the point of junction the canal is narrowed, and to this portion the term *neck* of the capsule has been applied. Commencing at this neck, the canal, situated in the cortical substance, becomes tortuous, of considerable size, and is then designated the *contorted tube*, conformably with its physical characteristics. It is in these tubes, as we shall subsequently see, that the most important phenomena of urinary secretion occur.

After a short course

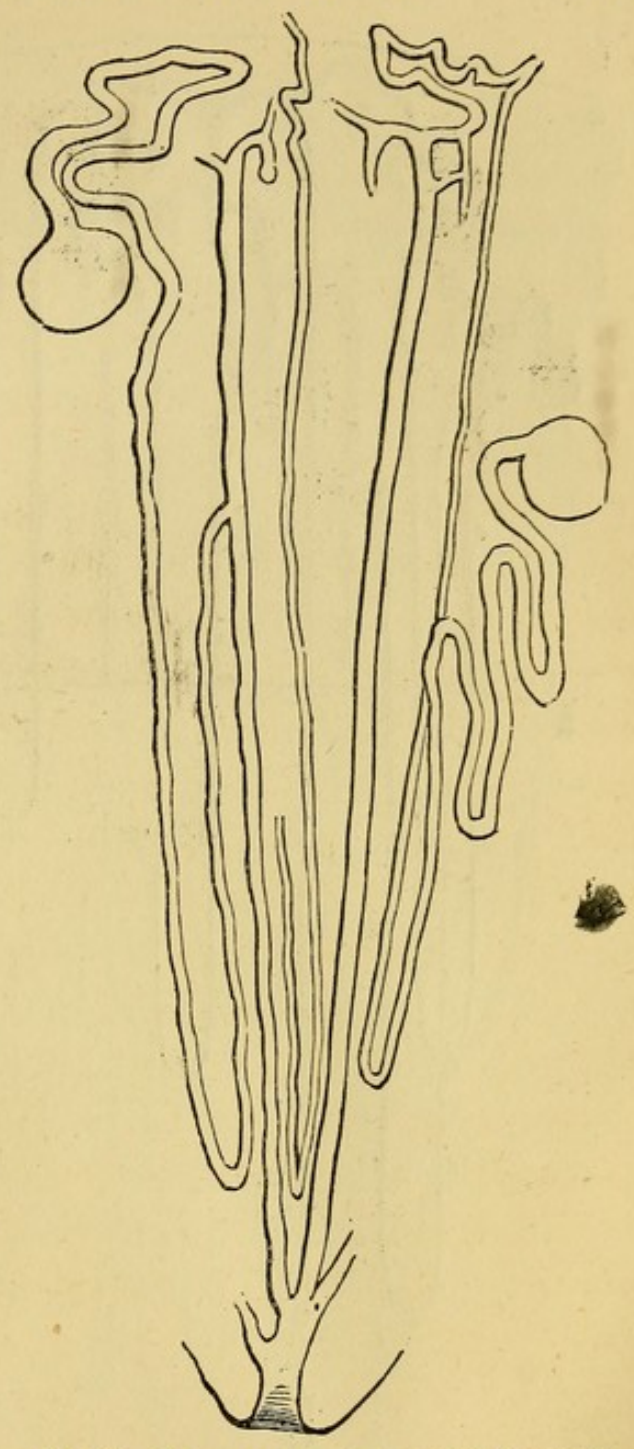

FIG. 2.—DIAGRAM OF THE LOOPED URINIFEROUS TUBES, AND THEIR CONNECTION WITH THE CAPSULES OF THE GLOMERULI.—*(From Southey, after Ludwig.)*

In the lower part of the figure one of the larger branching tubes is shown opening on a papilla; in the middle part three of the looped small tubes are seen descending to form their loops (their *relative size* is not so well indicated here as in Gross's figure on the following page. The ascending branch is about thrice the size of the descending.), and re-ascending in the medullary substance; while in the upper, or cortical part, two of these tubes, after some enlargement, are represented as becoming convoluted, and dilated in the capsules of the glomeruli.

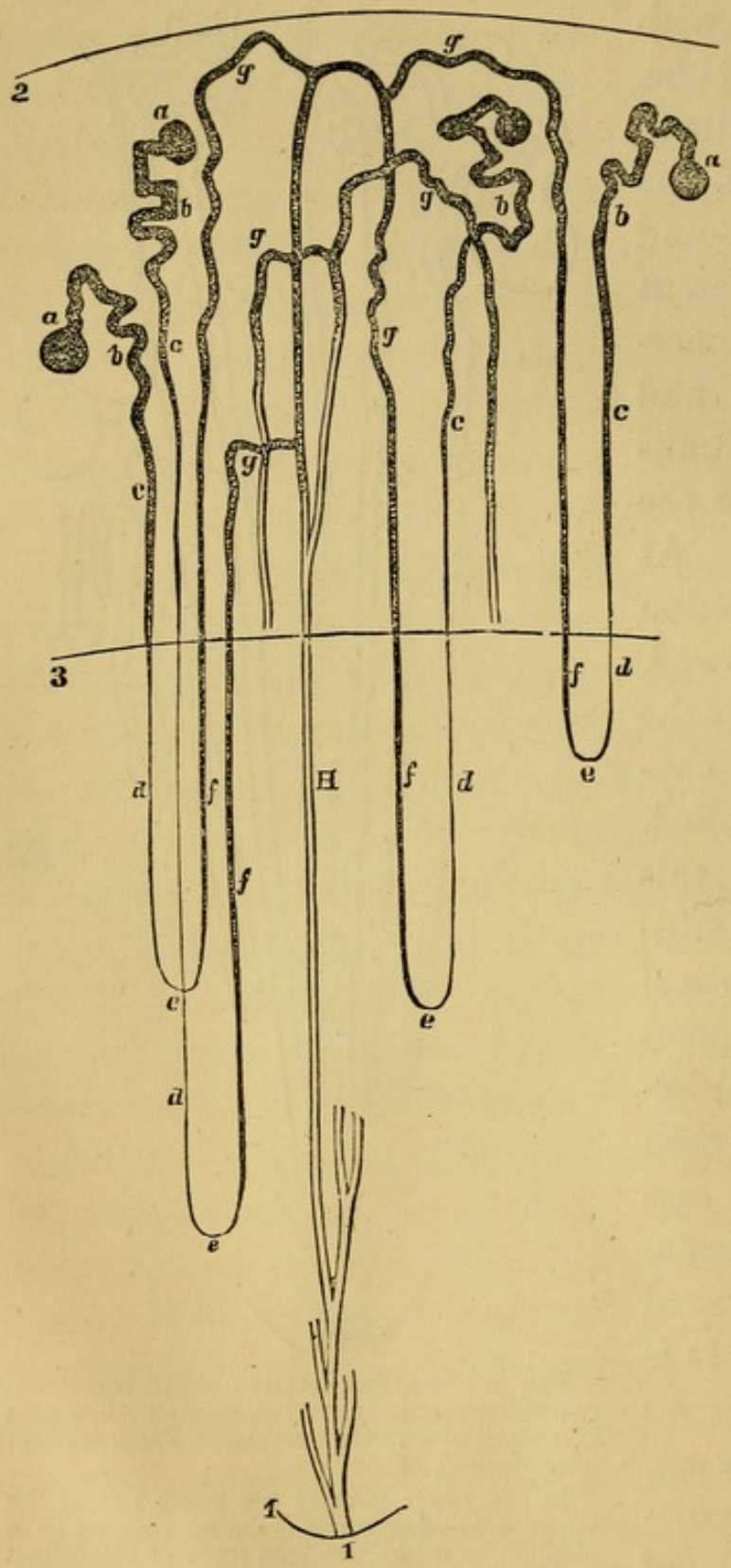

FIG. 3.—DIAGRAMATIC VIEW OF THE LOOPS OF HENLE SHOWING THEIR CONNECTION WITH THE MALPIGHIAN CAPSULE.—*(After Gross of Strasbury.)*

1 Surface of the papilla; 2 Surface of the kidney; 3 Commencement of the medullary portion (between 2 and 3 indicates the extent of cortical substance); *a a* Glomeruli of Malpighi; *b b* Tubuli contorti; *c c* Loops of Henle; *g g* Canaliculi, uniting to form the canal of Bellini—the latter unite with others to form a common canal opening on the summit of the papilla.

as a contorted tube, the canal becomes narrowed, and forming a straight canal descends towards the papilla; this portion is termed the *descending branch* or the *small branch* of the loop of Henle; within a variable distance of the papilla the canal abruptly bends back upon itself, forming an *ascending branch*, or *great branch* of the loop of Henle, which, running parallel with the smaller one, ascends to near the capsule of the kidney. At

this part of its course the canal undergoes a dilatation, and near the surface of the kidney the tubules anastomose with one another, occasioning a network appearance.

The Intermediate Portion (Schalstück, Schweigger-Seidel).—From the intermediate portion the *canal of union* arises, and under the name of *collector canal*, having previously united with other canals of the same nature, it opens by a common orifice of from 1-100th to

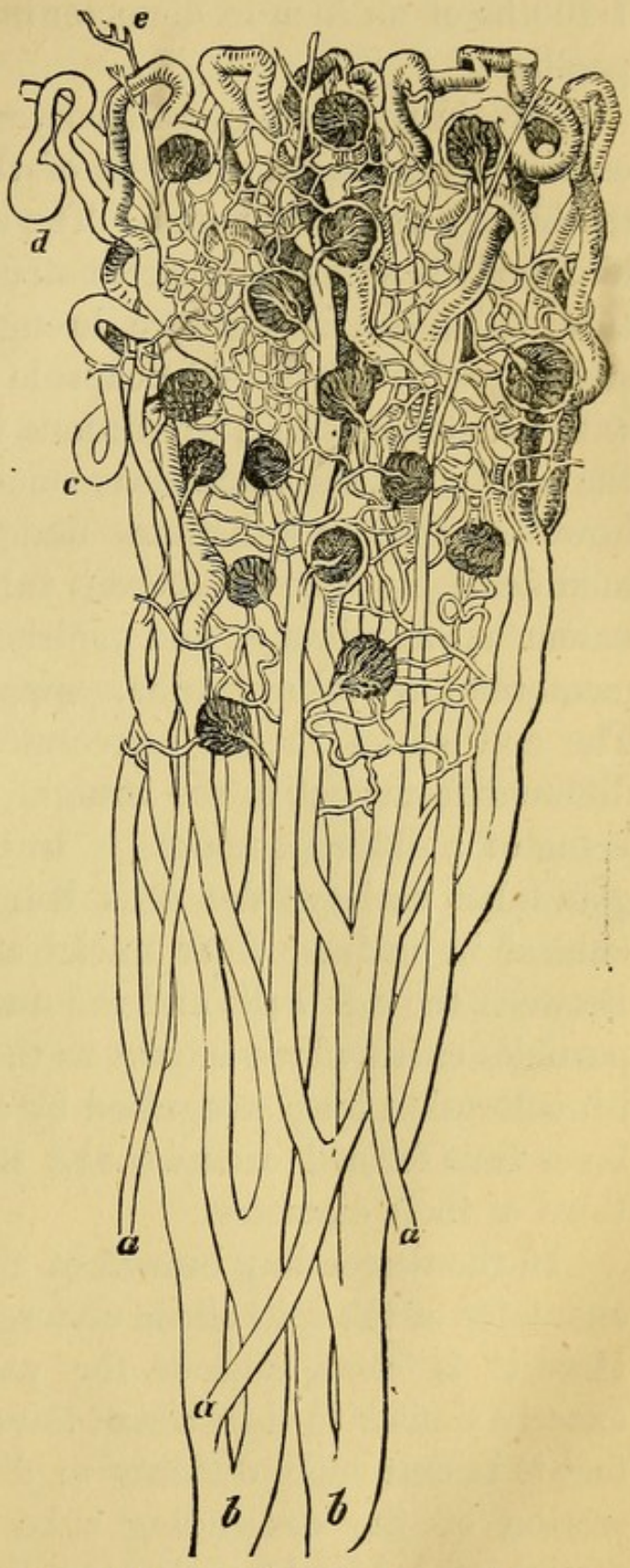

FIG. 4.—DIAGRAMATIC REPRESENTATION OF A PART OF THE STRAIGHT AND CONVOLUTED URINIFEROUS TUBES WITH THE GLOMERULI. — *(From Frey, after a drawing by Müller.*

b b Two large straight tubes in the medullary substance of the pyramid; *c* Convoluted tubes, several of their terminations in the Malpighian capsules, as in *d*; *a* Three arteries passing up the pyramid, and dividing into branches to the glomeruli; the efferent vessels are also represented, and the network of capillaries between them and the veins.

1-200ths of an inch in diameter into the summit of the papilla.

Certain peculiarities of structure, bearing intimately on the physiological purposes of the several portions of the kidney are to be noted. The capsule of the Malpighian body is without apparent structure—homogeneous. Internally,—an appearance brought out especially by staining with silver,—the capsule is found to be lined with an endothelium continuous with that which lines the neck. At the commencement of the *tubuli contorti*, however, the endothelium undergoes an important modification. The uriniferous tubes are composed of a basement membrane and epithelium—the basement membrane a thin lamina, apparently homogeneous. The epithelium in the convoluted tubes is essentially different from that in the straight, its physical relations being of a different nature. In the former it is of the glandular variety, the cells being large, angular, or cubical in outline; their nuclei are not very apparent. Between the cell walls and the nucleus minute granular particles exist, which impart to the epithelium a yellowish coloration long recognised by anatomists. The cell-layer thus formed occupies the tubes from a half to a third of their diameter.

In the descending branch of the loop of Henle, the character of the epithelium undergoes an abrupt change. Here it is clear, and of the pavement variety, and exactly similar to that which lines the blood-vessels; in fact it is extremely difficult to distinguish a transverse section of the descending tube from the transverse section of a blood-vessel. On the other hand, in the greater branch of the loop of Henle, the epithelium is exactly analogous to that which exists in the convoluted

tubes. The lining membrane of the convoluted tubes is continuous with that of the pelvis of the kidney, but it *entirely disappears* in the Malpighian capsule, so that the blood-vessels within the capsule are in direct contact with the cavity of the urinary passages. In the case of the lower animals the interior of the capsule is lined by cilia which propel the current of fluid toward the orifice of the tube, and this is probably the case in the higher animals also. Such an arrangement, therefore, is well adapted for the separation of the fluid and saline constituents of the blood, as we shall see in the sequel, the watery portion being probably separated by simple filtration in the Malpighian capsule, and the saline through the instrumentality of the cells lining the convoluted tubes.

In the *intermediate* portion the epithelium is clear, and resembles cylindrical epithelium, only it is flatter (Schweigger-Seidel, Henle). The *collector canals* of the kidney are thus distinguished by a clear epithelium applied against a membrane with a simple outline; as the tubes are distant from the capsule the epithelium becomes flatter, and the canals proportionately larger; deeper, the epithelium is cylindrical and the canal proportionately smaller.

With respect to the *connective tissue* of the kidney, the opinion was first enunciated by Goodsir that the elements of the cortical substance were thus united. This view was afterwards combated by Von Wittich, who maintained that the interstices of the secretory and excretory portions of the kidney were separated merely by the capillary vessels. This opinion held ground, especially among the German histologists, until Arnold Beer, in 1859, published his work "On the Connective

Tissue of the Human Kidney, in its Physiological and Pathological Conditions." The existence of connective tissue is now universally admitted.

The *lymphatics* of the kidney have been specially studied by Ludwig and Zawarykin. These vessels well formed, and frequently with valves, are found on the capsule of the kidney, and on the arteries and veins which form the hilus. Those of the capsule are in communication with a network occupying the thickness of the capsule; and that network, again, communicates with the interspaces in the cortical substance, between the *tubuli contorti* and the blood-vessels. According to Ludwig, the *tubuli contorti* are never in absolute contact with one another, but are separated by a cleft, containing a quantity of liquid of similar composition to that of lymph.

In the prolongations of the pyramids the lymphatic interstices are rare. They are still more rare in the medullary substance, where they are found only in the vicinity of the straight tubes. The lymphatic spaces of the cortical substance are thus in communication with those of the capsule and hilus.

Circulation of Blood in the Kidney.—As in the case of the liver the vascular arrangement of the kidney is peculiar. It is from the *arterial* blood passing through the kidney, and not from the venous, that the urea and other saline constituents of the urine are separated. Consequently, the arterial blood with which the kidney is supplied is impure in respect of its holding in solution these several constituents. The question where the formation of urea takes place will form the subject of further inquiry and deduction. Urea, suffice it to

remark at present, is undoubtedly a product of the metamorphosis of nitrogenous material, either of the body or circulating in the blood, and while it is highly probable that in its earlier form it is one of the results of direct oxidation in the depths of the tissues, there is, I think, sufficient evidence to regard the liver as the seat of its complete formation.

The presence of urea in the blood was first demonstrated by Bostock. This was confirmed by Christison in 1839, and by Wilson *(London Medical Gazette)* in 1833. That urea is not formed by the kidney, but simply filtered from the blood, has been shown by such experiments as those of Prevost and Dumas in the case of nephrotomised animals, in which urea notably accumulated in the blood; and M. Picard, of Strasburg, in his thesis on the subject at issue, proved that the blood in the renal artery contained a half more urea than that leaving by the emulgent vein (the artery, 0·040, the vein, 0·020). The renal artery, in passing into the substance of the kidney, breaks up into terminal branches, which, with the exception of the *vasa recta*, correspond in number to that of the Malpighian capsules. On reaching the Malpighian capsule the afferent artery pierces its homogenous envelope and breaks up into smaller tortuous branches, which ultimately unite to

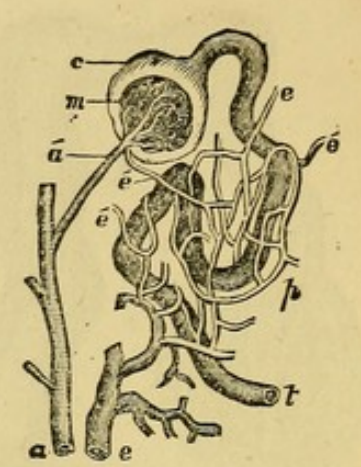

FIG. 5.—DIAGRAM SHOWING THE RELATION OF THE MALPIGHIAN BODY TO THE URINIFEROUS DUCTS AND BLOOD-VESSELS.—*(After Bowman.)*

a One of the interlobular arteries; *á* afferent artery passing into the glomerulus; *m* Vascular tuft formed within the glomerulus; *c* Capsule of the Malpighian body (capsule of Bowman) forming the termination of and continuous with *t*, the uriniferous tube; *é é* efferent vessels which subdivide into the plexus *p*, surrounding the tube, and finally terminate in a branch of the renal vein *p*.

form an efferent vein, which makes its exit from the capsule near the entrance of the artery, and unites with the inter-tubular venous plexus surrounding the convoluted tubes, all of which ultimately join the renal vein. Of the *vasa recta*, some are efferent veins which leave the Malpighian bodies close to the pyramids, pass out-

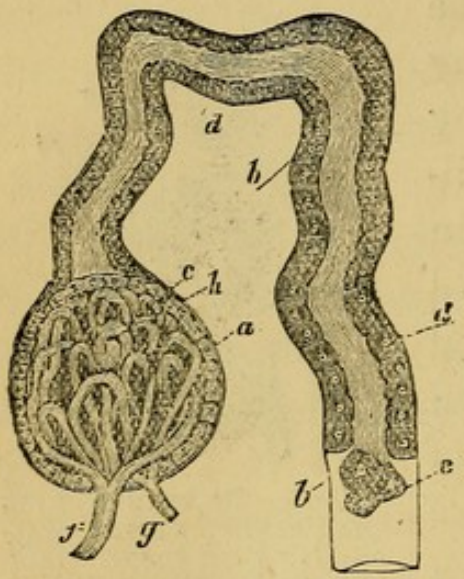

FIG. 6.—SEMIDIAGRAMATIC REPRESENTATION OF A MALPIGHIAN BODY IN ITS RELATION TO THE URINIFEROUS TUBE.—*(From Kolliker.)*

a Capsule of the Malpighian body continuous with *b*, the *membrana propria* of the coiled uriniferous tube; *c* Epithelium of the Malpighian body; *d* Epithelium of the uriniferous tube; *e* Detached epithelium; *f* Afferent vessel; *g* Efferent vessel; *h* Convoluted vessels of the glomerulus.

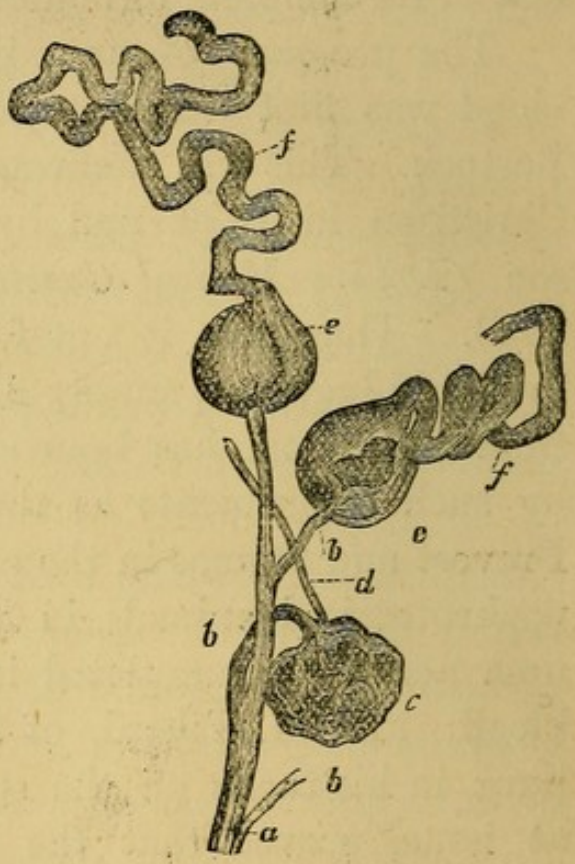

FIG. 7.—THREE MALPIGHIAN CAPSULES IN CONNECTION WITH THE BLOODVESSELS AND THE URINARY TUBES OF THE HUMAN KIDNEY.—*(From Kolliker, after Bowman.)*

a Termination of an intertubular artery; *b* Afferent arteries; *c* A denuded vascular glomerulus; *d* Efferent vessel; *e* Two of the glomeruli enclosed by the Malpighian capsules; *f* Uriniferous tubes connected with them.

wards between the straight tubes, and are united by capillaries with the returning veins, which follow a parallel course, and ultimately join the renal vein. Besides these, however, according to Virchow, Beale, and Arnold, *arterial vasa recta* are given off direct from

the afferent artery, and pass outwards between the tubes of the cones, and terminate in a capillary network surrounding them. The vascular arrangement is thus analogous to that of the bronchial arteries in the lungs, and the branches of the hepatic in the liver. It is inferred, therefore, and I think, as we shall see by-and-by, with the best possible reasons, viewing the structure of the kidney, that only the watery portion of the urine is removed by the Malpighian tufts, while the solid constituents are removed by means of the cells lining the convoluted tubes. Hence the salines must still exist in the inter-tubular capillaries after the blood has traversed the Malpighian capsules. This view harmonises, as we shall see, with pathological considerations. It will be obvious, then, that secretion of urine by the kidney must be influenced in obedience to the law of osmosis. Thus, the blood in a state of health has a specific gravity of 1055, is loaded with a certain amount of solid matter in addition to its serum, and the urine in health exhibits a corresponding constancy of composition; but given certain deviations in the blood from the normal standard, and both the secretion and the composition of the urine must present relevant diversity.

The precise mode in which urine is secreted must be, I assume, as follows: The watery portion transudes through the thin wall of the Malpighian capsule, its saline constituents are separated by the cells lining the convoluted tubes, and the watery portion, in passing over the cells, appropriates their contents by a process of solution, dissolving at the same time the cell walls.

This view has been confirmed quite recently in a highly instructive manner by Heidenhain. The living kidney manifests a strong and special affinity for indigo;

If a weak solution of sulphate of indigo and soda be injected into the viscera of a living animal, the urine and kidney soon present a blue coloration more or less pronounced, while no other part of the organism is similarly affected. The kidney therefore concentrates upon itself, and thus eliminates the colouring matter of the indigo. Further, there is a direct analogy between the separation, in this manner, of the colouring matter of the indigo, and that of the urea, uric acid, and other specific constituents of the urine. Directed by this analogy Heidenhain pursued his enquiries. Not only is the urine coloured by the blue of the indigo, but likewise certain portions of the kidney. If it be true, as Ludwig asserted, that the solid and aqueous constituents of the urine are separated entirely by the Malpighian tufts, the suppression of the secretion must necessarily have suppressed the elimination of the solid constituents. Heidenhain's experiments with indigo prove the contrary; for he was able to suppress the secretion of the aqueous portion of the urine without preventing the separation by the kidney of the colouring matter. The aqueous suppression may be determined in a twofold manner: by a large bleeding, whereby the arterial pressure is diminished; or by section of the spinal column above the bulb (Eckhard). If, into an animal in which section of the cord has been thus practised, a solution of indigo be injected, the following results are obtained, artificial respiration being at the same time practised: Not the least particle of urine reaches the bladder, yet the colouring matter passes into the kidney. But, differently from what obtains in the normal state, instead of being general in the renal structure, it occupies only a portion of it—the cortical substance. The portions coloured are: 1st, The convoluted

tubes; and, 2nd, The ascending branch of the loop of Henle. On the other hand, the Malpighian capsule and the descending branch of the loop of Henle did not present the slightest trace of coloration. The coloured parts, it will be observed, are those portions of the kidney which present the dark ciliated epithelium of secretory organs. Furthermore, the particular portion of the kidney, in which the elimination of the colouring matter takes place, is more exactly demonstrable. If the animal had been sacrificed ten minutes after the injection, it was found that the colouring matter had impregnated only the epithelial cellules, to the exclusion of the protoplasm, the nuclei; and the ciliæ, and the canal of the tubes were free from colour. If, on the contrary, the animal was killed an hour or so after the injection, the epithelial cellules were found discoloured, and the blue matter was found to have passed into the canals of the tubes, where, owing to the absence of water, it was found existing as a crystalline deposit. In the normal condition, there is every reason to believe, then, that the solid constituents of the urine are eliminated in a similar manner. To the extent that secretion of water continues the colouring matter distances from the primary seat of elimination; that is to say, it is found in the descending branches, in the collector canals, and finally, in the urine itself. This is what takes place in the normal state; shortly after a very small injection, all the portions of the kidney with the exception of the glomeruli become coloured; but the coloration soon ceases, and the colouring matter, removed by the water, passes into the urine.

Varying his experiments, Heidenhain obtained confirmatory results. Ligature of the ureter causes entire suppression of urine manner exactly contrary

to that which obtains in health. In about an hour secretion of urine is entirely suppressed; if at this period a solution of indigo be injected, the result is exactly the same as above detailed—that is to say, the coloration of the kidney is confined to the cortical substance and the ciliated epithelium.

If in the living animal the surface of the kidney be lightly cauterised by nitrate of silver in such a manner as to form transverse bands, and two or three days afterwards a solution of indigo be injected, the following results are obtained:—The cauterisation, in some manner of which explanation has not yet been given, causes suppression of water, in the portions of the kidney so acted upon, while in the portions not so operated on the normal physiological processes go on. On the contrary, in the cells of the cauterised parts the cortical substance is alone coloured; and miscroscopic examination demonstrates that the colouring matter impregnates only the convoluted tubes, and the ascending branch of the loop of Henle. That urea is secreted in this manner there is no room for rational doubt. Heidenhain found likewise, that if a strong solution of urate of soda was injected into the blood, it was found in the form of yellow granulations in the canals of the convoluted tubes, while the glomeruli did not contain a trace of it. In experiments in which the secretion of water was not completely suspended, these granulations were found in the collector canals; that these were not secreted there was shown by the fact of their larger size, and their presenting concentric laminæ deposited successively in their progress through the uriniferous canals. In birds, it will be remembered that the urine is solid, and is mainly composed

of granules of uric acid. According to Von Wittich, these granules exist in a rudimentary condition in the canals of the *tubuli contorti*, and even in the nuclei of the cells, but never in the Malpighian capsule (*Le Progrès Médical*, Sept. 5th, 1874.)

In order to the health of the body, or of any part of it, the first essential is a due supply of healthy blood. Not only must the blood be healthy, but the supply must be correlated to the necessity of the body or given organ. If depraved blood, *e.g.*, be presented to a secretory organ, the secretion thereof will not only be perverted, but the perverted secretion may in turn occasion structural changes. With a *diminished* supply of healthy blood atrophy may ensue, and the gland waste from inanition. To my mind, therefore, diseases naturally divide themselves into—(1), *Such as are occasioned by blood changes;* and (2), *Such as are due to conditions which influence the circulation even of healthy blood; and the latter subdivide themselves into* (a), *Influences acting from within the body, and* (b), *Morbid matters, or poisons, received from without.*

Parenthetically I may be permitted to remark here, as I have already endeavoured to show,* that even as it is essential to the existence of healthy blood that perfect depuration should take place, that while for this purpose special organs have special functions assigned to them, there being no such thing as perfect vicariousness of function, so are poisons eliminated by particular organs or structure of the body, so also are remedies eliminated; and the action of all remedies I

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* "Observations on Therapeutics and Disease."

take to be simply a modification of their toxic influence. We must make certain whether this toxic influence operates healthwards or diseasewards, relatively, not to health, but to the *diseased condition*.

Given an adequate circulation of healthy blood through the kidney, we have normal secretion and a healthy kidney. But, in the first place, what happens if we have inadequate circulation, and how may this be brought about? The circulation of blood is immediately under the influence of the nervous system, subject to the integrity of the hydrostatic purposes subserved by the valvular arrangement of the heart and veins.

The nervous system is threefold in composition: sensation is appreciated through the medium of the sensory nerves, intelligent impulse co-ordinates with the motor, and it is the special function of the sympathetic to regulate and control these actions, termed organic, and usually placed entirely beyond the control of the will. The organic functions may be enumerated as those of circulation, respiration, secretion, and excretion. It is with the first of these that we are at present concerned.

To M. Claude Bernard, to whom scientific Medicine is so much indebted, we owe the greater part of our knowledge relative to the special functions of the sympathetic. By Bernard's well-known experiment of dividing the sympathetic in the neck of the horse the following facts were disclosed: Considerable elevation of temperature took place on the injured side, though the whole body partook more or less in the rise of temperature, and the same side was bathed in perspiration. Bernard also noted that by division of the sympathetic

in the neck of the rabbit an elevation of temperature amounting to 7° Fahr. ensued on the side operated on, and, as in the corresponding case in the larger animal, the whole body partook in the rise of temperature. Fear may occasion diarhœa, enuresis, blushing, &c. What is the real cause of this? Simply that the tonicity of the arterioles has been diminished by a species of paralysis of the sympathetic, and especially of the fibres of Remak. The phenomena of Bernard's experiments, and those effects, as arising from mental emotion, are parallel in mode of causation.

The *tubuli contorti* of the kidney, as we have seen, are surrounded by special capillaries, to which the ultimate fibres of the renal plexus have been traced. Now, Moreau pointed out in 1868 that section of the splanchnic was followed, as in cholera, by an intestinal flux; and Eckhardt, in experiments which he performed on the splanchnics, found that section of them induced hyperæmia of the *tubuli contorti*, albuminuria, and increased secretion of urine.

Hyperæmia of the kidney occurs, likewise, in consequence of spinal paralysis, and particularly when the ganglionic nerves are affected. A torpid condition of the sympathetic is characteristic of certain states of insanity, in which we have abdominal plethora, as in paraplegic cases; and is the profuse salivation of idiocy not familiar enough, and likewise thus explainable?

Recently, again, Prof. Vulpian, in a communication to the Société de Biologie of Paris, stated, as the result of observations on a dog subjected to the influence of woorara, that division of the left splanchnic nerve was followed by congestion of the corresponding kidney; it assumed a deeper hue, enlarged slightly, and polyuria

and albuminuria supervened; but without extravasation of globules of blood or desquamation of the tubes. At the same time, what is specially interesting, the renal vein became larger and redder. On the peripheric end being subjected to the action of electricity the kidney and its capsule became pale. They progressively resumed their reddish hue as the passage of the current was suspended, while the size of the renal vein diminished. Just as section of the splanchnic operates on the *tubuli contorti*, Dr. Basham narrates the case of a shoemaker subject to attacks of hæmaturia, which always recurred from grief at a drunken wife's misconduct; and Rayer mentions a case of hæmaturia as a sequel of a fit of passion.

Supposing an individual to have been respiring the atmosphere of a heated room for several hours, and he suddenly exposes himself to the influence of a much colder atmosphere, what is likely to happen, and does frequently happen? A paralysing influence is made on the cardiac and pulmonary plexuses of the sympathetic, congestion ensues, and the heart, freed to a certain extent from the controlling influence of the sympathetic, beats more vigorously and more quickly, and inflammation may be established. Supposing a person to have been exposed to the continuous influence of cold or damp on the loins, a similar impression is made on the splanchnic nerves: congestion of the *tubuli contorti* ensues, the normal correlation of the interrupted blood towards the vessels and tissues is altered; inflammation thus supervenes with the train of symptoms whereby we recognise acute nephritis.

It may be mentioned here, to avoid further reference to it, that albuminuria may take place from static con-

gestion, independently of any special affection of the kidney; thus, in cases of valvular diseases of the heart, affections of the liver, and in cases of pleuritic effusions, as we have seen in the hospital. The occurrence of transitory albuminuria in pregnancy is sufficiently familiar to every one, and its cause is equally evident.

Albumen may likewise be found in the urine when the blood contains too much water, or a diminution of albumen, conditions termed respectively hydræmia and hypalbuminosis.

It is interesting to note that gastric juice seems to exercise an influence of a peculiar nature over albumen, though it is alleged that a highly albuminous diet causes the appearance of albumen in the urine, for when Bernard and Barreswill injected albumen dissolved in water into the jugular veins of dogs they found it in the urine three hours afterwards; but if before its injection it was mixed with gastric juice they failed to discover it.

Such, then, appears to me to be the etiology and initial pathology of what may be termed idiopathic nephritis. But I have postulated that blood changes may likewise induce structural changes—may cause in this case what I may venture to term, in contradistinction to the *idiopathic* variety, *sympathetic* nephritis.

With the symptoms of simple nephritis we are not at present concerned. If it be true, *cæteribus paribus*, that healthy blood and normal circulation imply healthy repair and healthy secretion, it follows as a corollary that impure blood and deranged circulation will occasion depraved secretion and structural change. What I have elsewhere ventured to term the *material correlation* of the parts is altered, with morbid changes as a result.

From this point of view we recognise certain condi-

tions of the system induced, or idiopathic, which lay the foundation of disease of the kidney and liver, as well as of other glands. Pathologically, their features are strikingly identical, and they divide themselves naturally into changes of the basis structure of the several glands, and of their special secretory apparatus. I hold that these conditions, their prevention, and the cure of derangements induced by them, are paramount in importance to the ultimate pathological changes, for when the time has arrived for the amusing wranglings to which we are so frequently entertained over microscopic peculiarities, medical science has entered upon a phase of little avail to the patient. I am far from denying that minute pathology is incapable of throwing light on deviations from health, but I am persuaded that too frequently time, talent, and energy are dissipated upon it which might have been employed to better purpose, both for the cause of Medicine and the benefit of humanity.

LECTURE II.

Chronic Nephritis and "Bright's Disease"—Hippocrates on Dropsies—Cruickshank's differentiation of Dropsies—Etiology of Cachectic Nephritis—Divisions and Varieties of Bright's Disease so-called; of Christison, Martin-Solon, Rayer, and Johnson—The six forms of Rayer; their Pathological characteristics—Dr. Johnson's "small red-glandular Kidney"—"Large white Kidney"—"Granular fat Kidney"—The lardaceous, or waxy, Kidney—The contracted, or granular Kidney.

GENTLEMEN,—Chronic nephritis and Bright's Disease have unfortunately become synonymous terms in Medical literature. I am one of those who regret that the term Bright's Disease should convey such significance. The merit of Bright, so far as I can gather, seems to be that he recognised the presence of albumen in the urine as being frequently associated with peculiar structural changes of the kidney.*

Hippocrates distinctly refers to the relation of certain dropsies with renal affections. His remark is to the following effect:—"That the dropsies supervening on acute diseases are all serious, for they do not dispel the fever, they increase the pain, and conduce to death. Certain of them arise from *the flanks and loins*, others *from the liver*. In the first *the feet swell*, and there is also obstinate diarrhœa, which does not diminish the

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* "La découverte de M. Bright a essentiellment consisté à rapprocher ces trois choses, l'hydropisie, la coagulabilitié de l'urine, et l'affection des reins, dont en même temps, il a trouvé les caractères spéciaux."—RAYER.

pain of the flanks or loins, and does not empty the abdomen." (Gardiel, French Translation of Hippocrates, 1801.)

Galen, Aetius, Avicenna, and many others of the ancient and mediæval writers, were quite familiar with the association of dropsy with renal affections. It is, however, to Cruickshank, in 1798, that the merit is due of having taken the presence of albumen in the urine as the basis for an important distinction in cases of dropsy. He pointed out that by heat and nitric acid the presence of albumen in the urine could be demonstrated, and that dropsy from kidney disease was thus distinguishable from that depending on diseases of the other viscera—a fact which, speaking generally, may be held to be correct.

Then follow the researches of Blackall, Abercrombie, Alison, Gregory, and Bright in this country, and M. Solon, Rayer, &c., on the continent. I doubt very much if these authorities may not be held as having exhausted the pathological anatomy of the kidney, and if one solitary fact has since been added to this portion of the subject. Hardly less numerous are the designations of chronic nephritis, than the pathological appearances described by authors. I am not certain that the old term cachectic nephritis is not still the best that can be applied to the subject of our remarks. By Bright the disease was named *granular disease of the kidneys*, *renal disease accompanied with the secretion of albuminous urine;* by Gregory, *diseased state of the kidneys connected with albuminous urine;* by Christison, *granular degeneration of the kidneys;* by Martin-Solon and Willis, *albuminuria;* by Rayer, *nephrite albumineuse;* and by Copeland, *inflammation of the Malpighian capsules*, &c.

Etiology of Cachectic Nephritis.—Authorities are pretty much agreed that the following constitute the predisposing causes of cachectic nephritis: Cold, damp, scrofula, syphilis, gout, mal-assimilation and unwholesome food; scarlatina, possibly other constitutional diseases, and *par excellence*, inordinate indulgence in alcoholic liquors.

I shall endeavour to show, in the sequel, that what we usually designate Bright's Disease is *not* a disease peculiar to the kidney, but the local expression of a *constitutional* diathesis, manifesting itself in other organs as well.

Divisions and Varieties of Bright's Disease.—Rokitansky describes eight varieties of cachectic nephritis; Christison has admitted seven; Martin-Solon has adopted Rayer's classification, only that he combined his (Rayer's) fourth and fifth form; Bright described three forms, which M. Rayer thinks corresponded to his third, fourth, and sixth varieties, and he has indicated another, or first form; Johnson may be said practically to have recognised three forms. It seems to me a matter of secondary importance how pathological appearances may be arbitrarily grouped, providing a proper conception of their nature is possessed. I look, then, upon simplicity of classification as a desideratum; however, as Rayer's classification may be regarded as occupying an intermediate position in this relation, I present you, in the first place, with an outline of it.

First Form.—The kidney is enlarged; in the adult the weight may vary from eight to twelve ounces instead of four, the normal weight. The consistence of the organ is greater, but there is no hardness; the kidney seems as if injected with water; its surface is of a mor-

bidly red colour, and spotted over with a number of red points of a deeper colour than the rest of the organ. On section of the kidney it is found that the augmentation of volume is of the cortical portion; in the interior of the organ are found numerous red spots corresponding to those on the cortical surface, and which appear to be Malpighian capsules highly injected with blood. This appearance is admirably displayed in Bright's Plate I., Fig. 1. The tubular substance is compressed between the tumefied prolongations of the cortical substance, and presents a duller red appearance, and the striæ are less apparent than they are in health. The mucous membrane of the calyces and the pelvis is injected, and presents vascular arborizations on its surface. This form is rarely observed, as death seldom takes place until the disease has considerably advanced. This hyperæmic condition must be distinguished from that which is sometimes witnessed in cases of heart disease, and in cases of simple nephritis, in which the kidney is red and harder, and almost always presents some purulent spots.

Second Form.—The weight and volume of the kidney are augmented, as in the preceding variety, but the consistence of the organ is less. The tubules are frequently more distinct than in health; but that which *specially* characterises this form is a mixture of anæmia and hyperæmia, whereby the surface of the organ presents a mottled aspect, the red blotches being disseminated over a yellowish-white ground. On section the cortical surface is found swollen, and presenting a pale yellowish aspect tinged with red, and strongly demarcated from the tubular substance by the difference of colour, the latter being reddish-brown.

Third Form.—The volume and weight of the kidney are increased, as in the preceding varieties, but neither the red patches nor the marbled appearance exist here. On section, the cortical substance appears of a tolerably uniform pale colour; in some cases it is so pale as to resemble the flesh of an eel. On certain points of the surface small vessels injected with blood are observed; more rarely small patches of a brownish colour or large granulations are noticed, or depressions, proving an old deposition of plastic lymph. Frequently hard red indurations of the papillæ of the tubular substance are discovered. The mucous membrane of the pelves and calyces is sometimes thickened, and here and there injected. These lesions are, however, not characteristic in a special manner, being found as well in simple nephritis.

Fourth Form.—This form has been designated by Bright "the granulated texture of the kidney"—granular fat kidney of Johnson (Bright's Plate III.) The size and weight of the kidney are still increased; the external surface is frequently of a pale yellow colour, and covered with minute spots of a milky-white or yellowish hue. The designation yellow granular matter, hardly gives an exact idea of the appearance in question. These spots are about the size of a pin's head, sometimes elongated, and resemble the particles in whey; they are all covered, as if it were by a thin coat of varnish. The cortical substance is swollen, and occupies a larger space than in health, particularly between the cones. Bright's granulations are found in the depth of the cortical substance. On dividing the organ from its convex border towards the pelvis the cortical substance offers, as in the second and third forms, a general pale yellow

appearance, contrasting strongly with the red appearance of the tubular substance. The little milk-white granulations, in place of being more or less rounded, and separated the one from the other, as ordinarily happens, on the surface of the kidney, appear in the form of irregular lines, flocculent, and seem to be continuous with the divergent striæ of the tubular substance. If the section be carefully made in the direction of the striæ of the tubular substance that disposition is very apparent, particularly at the periphery of the kidney and base of the cones, where the granular alteration is generally more strongly marked.

Sometimes but few granulations are observed in the depth of the cortical substance, while they may be sufficiently numerous on the surface. In other cases, on the contrary, the granular alteration invades all the depth of that substance on to the little prolongations which penetrate into the base of the tubular cones, of which the striæ are separated and drop like a plume of feathers or a sheaf of corn (third form of Rokitansky). If the kidney be macerated the granulations become more distinct; their dull white colour becomes more obvious against the surrounding cortical substance.

In the kidneys of infants dying from dropsy with albuminous urine, Rayer has found these granulations larger and rounder than ordinary.

Fifth Form.—This form is more rare than the preceding; the kidneys are also larger and heavier than in health, and their lobules are more marked. They appear on the surface as if small grains of semolina were scattered under their proper cellular investment. These minute grains seem to be Malpighian corpuscles, enlarged by albuminous infiltration, and are distinct from the

yellowish patches which are sometimes observed in the cortical substance—small granulations of lymph found in this and other forms of nephritis. Dropsy in this, as in the other forms of the disease, appears frequently during life.

Sixth Form.—Rayer thinks this form to correspond with the third variety of Bright; the kidneys are sometimes larger, but often smaller than in health, are hard, and present inequalities or tubercules on their surface. Few or none of the milky granulations are found on this surface; but on section of the organ a certain number are always found in the depth of the cortical substance. Rayer mentions that he has seen a kidney, indurated and irregular, present on its surface a great number of the granulations of Bright. In other analogous cases, however, he adds, he has vainly sought for the granulations of Bright, if that term be not applied to the little projections ordinarily scattered on the surface of the kidney. More frequently, however, the kidneys are decolorised in a general or partial manner, and present in their pathological bearings such a resemblance to the disorganisations due to simple chronic nephritis that it would be impossible to draw any distinction, if the symptoms during life were not taken into consideration. In the advanced stages of the disease the investing membrane is almost always thickened, at least in many parts, and very adherent to the surface of the organ.

Dr. Johnson divides chronic nephritis into the following pathological varieties:—

1st.—*The small red granular kidney*, of which, by the way, Bright gives no representation. At no period of the disease, according to Johnson, is there enlargement

of the organ, but from the commencement a process of wasting sets in. In the early stages, when death has occurred from some other disease, the capsule is found adhering firmly to the surface of the gland, so that it is difficult to tear it off without bringing away some of the glandular tissue. The fine lobular markings are less distinct than in the normal state, and the surface of the kidney is slightly uneven and granular. As the disease advances there is progressive wasting of the glandular portion of the kidney, with granular unevenness of the surface and diminution of the thickness of the cortex, so that by degrees the bases of the medullary cones approach nearer to the surface of the gland. In extreme cases the kidney may be reduced to one-half, or even one-third of its normal size and weight. The cortical secreting portion of the gland is evidently the part chiefly implicated, while the medullary cones remain nearly intact. In all stages of the disease one or more, sometimes numerous, serous cysts may be seen projecting from the surface, and varying in size from a pin's head to a pea, sometimes as large as a filbert, or even larger. Even in the most advanced stage of the disease, the organ retains more or less of its normal colour and vascularity, and is thus designated the *red granular kidney*, in contradistinction to other varieties of Bright's disease.

On microscopical examination, the chief changes in the kidney (some of which dilute acetic acid brings out very well) are found in the convoluted tubes, in the arteries, in the Malpighian tufts and capillaries. The tubes may be abnormal, or be opaque and granular*

* This condition has been described by Valentin ("Examen. Microscopique des Granulations des Reins," p. 290, 1837) in the following terms:

leaving a clear central canal. Other tubes are perfectly denuded of their cells, while some are filled with granular matter held in position by coagulated fibrine. Atrophy of the tubes seems to be the immediate result of the removal of their gland cells, and the contraction of the interstitial tissue; and when it is remembered that the cell-layer occupies the tube to the extent of from a half to a third of its diameter, contraction of the organ, it will be apparent, will take place in a direct ratio to the desquamation of the cells. Under other circumstances, dilatation of the tubes takes place, and these dilated tubes, it would appear, form the cysts recognised by the naked eye in this variety of Bright's disease.

In other cases the tubes are filled by transparent cells with a single nucleus. In the most contracted

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"Les canaux droits (conduits urinifères) de la substance tubuleuse étaient vides ou ne contenaient qu'une petite quantité d'une substance très liquide; les conduits urinifères flexueux de la substance corticale étaient presque entièrement remplis par une matière d'un jaune-grisâtre, qui les injectait en quelque sorte, et les rendait très visibles. . . . . La substance jaune-grisâtre qui remplissait les conduits urinifères flexueux était comprisée de particules granulées irrégulières, de volume variable, de petites corps moleculaires, et de globules jaunes d'une forme ronde. Les canaux urinifères droits contenaient les mêmes élémens, seulement en quantité beaucoup moins grande."

The same granules Valentin found in the testicles and seminiferous tubes. M. Rayer remarks, with reference to the above, and the general view taken by Valentin: "M. Valentin s'est trop hâté, ce me semble, de faire une théorie générale de la maladie d'après l'inspection microscopique d'une de ses formes, et d'après une seule observation. M. Valentin dit que les vaisseaux sanguins et les corpuscles Malpighi n'offrent aucun changement, mais cette intégrité n'a pas lieu dans tous les cas, puisque j'ai observé et figuré grandules de Malpighi altérées et remplacées par de petites vesicules. . . . . D'un aure côté, les observations microscopiques de M. Gluge ("Anatomisch-Mikroscopische Untersuchung zur Allgemeinen Med. Spec. Path.," 1839) sur la maladie de Bright, ne s'accordent pas avec celles de M. Valentin. Suivant M. Gluge, la dégenerescence des reins consiste essentiellement en un trouble de circulation, dans les vaisseaux capillaires de la substance corticale, et particuliérement dans les glandules de Malpighi. Ce trouble, dit M. Gluge, est dû à un arrêt de la circulation; les corpuscles sanguins perdent une partie de leur substance, s'agglomerent et empêchent la marche due sang; de la, imbibition du serum dans les conduits urinifères urine albumineuse et hydropisie."

kidneys these cells are fewer; in others, again, they are

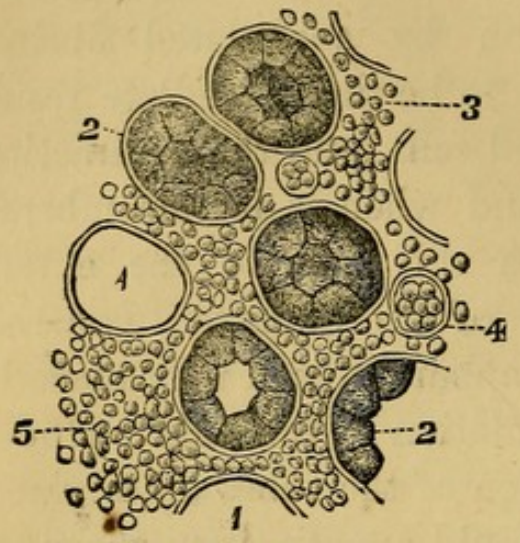

FIG. 8.—Transverse section of a portion of the kidney in a case of leucocythæmia. 1. Uriniferous canal denuded of its epithelium. 2. Uriniferous canal full of granular epithelium. 3. Longitudinal section of capillary full of white blood globules. 4. Transverse section of a capillary. 5. Mass of white blood corpuscles from a ruptured capillary—magnified 350 diameters.—*(After Ollivier and Rahvier.)*

FIG. 9.—Uriniferous tubes atrophied, containing small cellules in part disintegrated, and fatty granulations—magnified 420 diameters. Compare with Fig. 8 as to relative size, both being magnified to the same extent.—*(After Cornil.)*

very numerous; and Dr. Johnson believes that they have a special relationship with the cysts with which they are usually associated; and he thinks that dilatation of the tubes is to be ascribed to a watery secretion elaborated by these cells. It is more than probable, however, that the dilatation of the Malpighian capsules, and of the tubes into the form of cysts, is owing to the accumulation of urine behind a narrowed or obstructed tube; the former condition being caused, as already indicated, by the contraction of the surrounding interstitial tissue, and the latter by the presence of exudation material. The tortuous appearance of the medullary tubes in chronic nephritis is due doubtless to the same cause.

In other tubes, particularly in the cortex, fibrinous plugs are found, which, if discharged from their seat of formation, would have appeared in the urine as hyaline

casts. The basement membrane of the tubes is thickened; the Malpighian bodies are also thickened, and there is thickening of the walls of the minute arteries.

Dr. Johnson's *second variety* is the "*large white kidney.*"

Bright's Plate, Fig. 4, represents this form. A sub-division of this variety is "*the granular fat kidney.*" It presents the same general appearance, only that on section the surface of the cortex is found to be interspersed with numerous small yellowish opaque spots. (*Vide* Bright's Plate III., Fig. 3.)

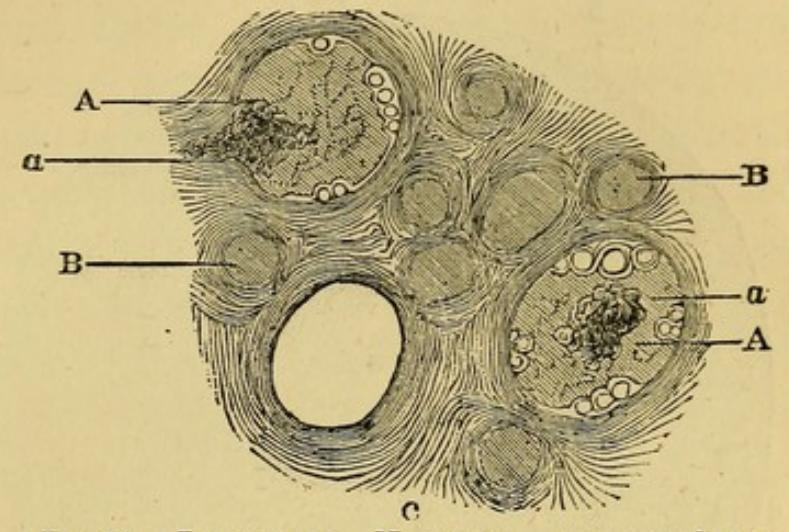

FIG. 10.—INTERSTITIAL NEPHRITIS, SHOWING COLLOID CYSTS OF THE KIDNEY.

A Small Cysts from the Distension of a Glomerulus; *a* Vestiges of Blood Vessels; B Uriniferous Tubes; C Connective Tissue of the Kidney increased—magnified 40 diameters.—*(After Cornil.)*

In the *third* subdivision of Johnson's *second* variety, the cortical portion of the kidney may be found more or less atrophied, with an uneven granular surface, the yellow specks of fatty degeneration being in some cases still visible on the surface and on section. "The difference between the

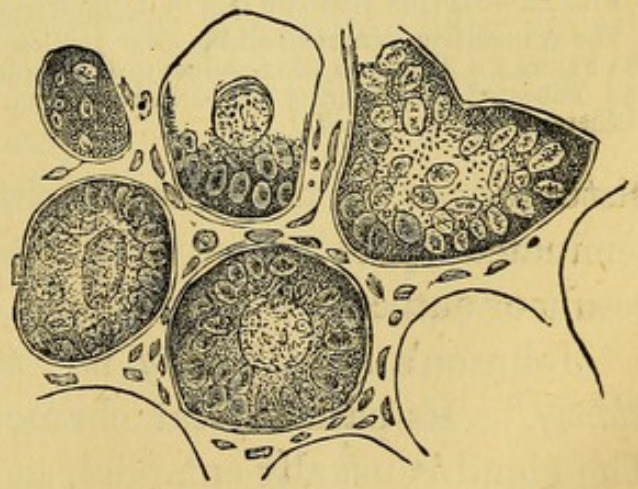

FIG. 11.—TRANSVERSE SECTION OF RENAL STRUCTURE IN A CASE OF BRIGHT'S DISEASE.

The cells are granular, being full of proteic and fatty granulations. At the centre of the tubes hyaline cylinders are observed.—*(After Cornil.)*

'*simple fat kidney*' and the '*granular fat kidney*' seems to be this: In the simple fat kidney there is a general fatty infiltration of the gland-cells in the cortex, and this is a primary change, and one always associated with the presence of albumen in the urine, and other functional disturbance; in the granular fat kidney there are disseminated spots of fat in the cortex, and this as the result of antecedent conditions."

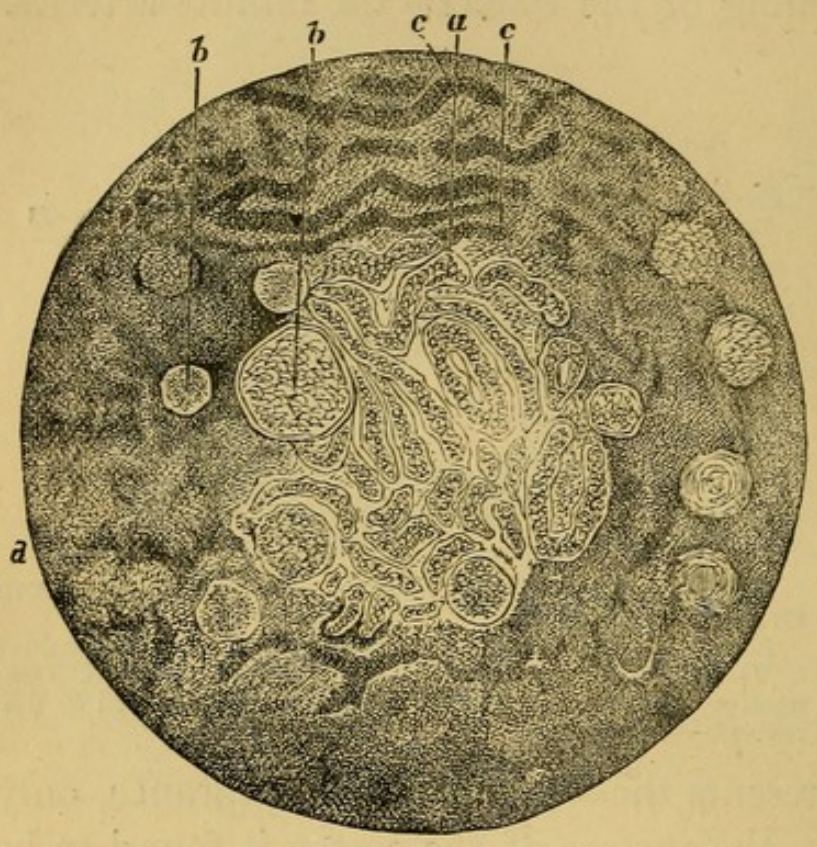

FIG. 12.—SECTION THROUGH ONE OF BRIGHT'S GRANULATIONS.
The granulation comprises all the clear portion in the centre of the Figure; *a* Tubes; *b* Glomerulus; *b d* Atrophied Glomerulus and Tubes of neighbouring Renal Parenchyma. Magnified 40 diameters.—*(After Cornil.)*

Johnson's *third variety* is "*the lardaceous, or waxy kidney.*" Its pathological characteristics are as follow: The gland is usually enlarged, sometimes very much so. The surface of the kidney is smooth and pale; the texture of the anæmic and thickened cortex is firm, and has the semi-translucent appearance of bees'-wax. The cones retain their normal colour, vascularity, and size. The cut surface presents numerous glistening points due to altered Malpighian capillaries. In some cases

minute yellow fat granulations are scattered through the cortex. This is the *large* smooth lardaceous kidney, and is usually associated with a corresponding condition of the liver and spleen. Sometimes atrophy follows upon enlargement; the cortical substance wastes, and coarse granulations appear on the surface. This is the *contracted or granular lardaceous kidney* (Bright's Plate III., Figs. 1 and 2.) The Malpighian capillaries are thickened, opaque, glistening, and wax-like. Some of the afferent arteries appear quite normal, others thickened by muscular hypertrophy ; but the greatest number appear more or less homogeneous, and wax-like. Their muscular structure appears to be concealed by a fibrinous infiltration. The *vasa recta* of the cones present a similar wax-like degeneration. On the addition of liquor potassæ the walls of such a specimen become transparent, so that the red blood corpuscles become visible through the thickened Malpighian capillaries, and the muscular fibres of the minute arteries are rendered quite distinct. Oil globules may be seen in the walls of the Malpighian capillaries; less frequently in the intertubular capillaries. Dr. Johnson has never seen thickening of the walls of the intertubular capillaries. Thickening of the basement membrane often gives the appearance of intertubular thickening. Virchow explains the pathological peculiarities of this variety of Bright's disease in the following manner: There exists thickening and degeneration of the minute arteries and Malpighian capillaries. In consequence of this degeneration, albumen and fibrinous material transude through the walls of the vessels, and infiltrate the tissues of the kidney. It has been suggested that the copious secretion of urine peculiarly characteristic

of the early stages of this form of renal disease is due to paralysis and dilatation of the minute renal arteries, consequent on degeneration of the walls. This explanation is disputed by Dr. Johnson. He states that while he never met with a single case of extensive change in the secreting structure of the kidney unaccompanied with thickening of the renal blood-vessels, he has examined many cases of lardaceous disease with only incipient degeneration of the blood-vessels. In proof thereof, Dr. Johnson quotes the following case, in which the two kidneys weighed twenty-eight ounces: The patient, at the time of his death, was twenty-one years of age. Since the age of three he had suffered from hip disease, with purulent discharge from several openings about the joint. For three or twelve years he had more or less dropsy, and for several months the dropsy had been general. The clinical history, the character of the urine, and the appearance of the kidney, were those of typical case of lardaceous disease of the kidney, yet the Malpighian capillaries and the arteries in these greatly enlarged, pale and wax-like kidneys were only moderately thickened.

Todd recognised the following divisions:—1st, An acute dropsy (nephritis of scarlatina); 2nd, A form in which the dropsy is very variable, and the progress of the malady slow, and comprising *fatty degeneration* (Bright's kidney), waxy degeneration, and chronic nephritis with atrophy of the kidney, the gouty kidney. Grainger Stewart adopts three forms: the inflammatory, the waxy or amyloid, and the cirrhotic or atrophic. Dickinson's classification is almost identical, and is based, in like manner, on the pathological anatomy of the part: 1st, Morbid alteration of the kidney, with

changed condition of the epithelium of the uriniferous tubes (tubal nephritis); 2nd, An altered condition of the fibrous tissue (contracted kidney); 3rd, An altered condition of the blood-vessels (amyloid and waxy degeneration.) Finally, Professor Sée (Leçons à l' Hôpital des Enfants, 1860-67) adopts, *(a)* The acute inflammatory (catarrhal) characterised by desquamation of the epithelium, &c.; *(b)*, The chronic form, comprising the fatty and amyloid degeneration, and atrophy.

LECTURE III.

Appearances produced by Disordered Circulation in the Kidney—Appearances produced by Cachectic Conditions of the Blood, and due to Perverted Chemical Changes—*Post-mortem* appearances of Simple Nephritis—Cachectic Nephritis a Blood Disease—Condition of the Blood in Cachectic Nephritis—Period of life at which Bright's Disease most frequently occurs—Amyloid Changes—Tube Casts: their signification—Relation of Epithelial Desquamation to the amount of Albumen and Salts in the Blood—Why is Dropsy not a common symptom coincidently with the "small red-granular Kidney?"—Causes of Cachectic Nephritis—Author's Classification of Diseases—Fatty Degeneration; its Nature—Fatty Livers of the Strasburg Geese—Relation of Fat to Fibrine, the Bile Acids, and Oleine and Margarine—Alcohol as a cause of Fatty Degeneration—Increase of Urea in the Blood in Cachectic Nephritis—Influence of the Liver on the production of Urea—Glycogen, Leucin, and Tryosin as Liver products—Fibrine: Simon and Lehmann's views as to its production—Decreased Temperature and Uræmia.

GENTLEMEN,—Such is an epitome of the divisions of Rayer, Johnson, and others. The pathological varieties seem to me more apparent than real; no matter how grouped, the appearances in question are resolvable into the following:—

1*st.*—*Appearances produced by Disordered Circulation in the Kidney*—

COMPRISING

Anæmia.	(a). Hyperæmia.	(b), Hypertrophy.	Inflammatory Agglutination and Contraction of Fibrine.
Ex-sanguine, eel-flesh colour. Atrophy.	Vascular arborizations. Injected Malpighian capsules; effusion of serum, albumen, blood, and coagulable lymph, and consequent tumefaction of cortical prolongations; interrupted circulation, and dropsy.	Thickening of fibrous investment of kidney, and enlargement of the organ. Increase of connective tissue, thickening of Malpighian capsule, and convoluted tubes.	Adherence of capsule of kidney. Contraction of the organ.

2nd.—Appearances produced by Mechanical Conditions—

Cysts of Tubes and Malpighian Capsules (more peculiar to Contracted Kidney).

3rd.—Appearances produced by Cachectic Conditions of the Blood, and due to Perverted Chemical Changes—

1. On Basement Structure of the Kidney.	2. On Secretory Structure of the Kidney.	3. On Vascular Structure of the Kidney.
Fatty Degeneration. Purulent Degeneration.	Fatty granular and amyloid degeneration of secretory cells; desquamation; consequent shrivelling; and disorganisation of the Malpighian capsules.	Thickening of muscular coat; fatty and lardaceous degeneration of walls of vessels.

If you remember what I stated to be the special properties of cells (*vide* page 13) you will at once appreciate how the above changes are induced. You will remember the conditions under which I stated that acute nephritis arose, and the intimate part in the pathological aberration which I ascribed to the nervous system. If acute nephritis go on unchecked it will produce structural changes, and in consequence, morbid degenerations, differing in no respect from that form of nephritis due to cachectic conditions of the blood.

What are the post-mortem appearances of simple nephritis? The Malpighian capsules are found red, or darkish, and larger than in health (Rayer's Atlas, first form of Néphrite Albumineuse, Plate VI., Fig. 1., and Plate X., Fig. 3); they become discoloured, especially at the time that the anæmia of the cortical substance becomes evident. In that advanced stage the Malpighian capsules resemble very small serous vesicles, interspersed with others which are a little larger, and which afterwards become true cysts. The ecchymosed patches, or *petechiæ*, which are sometimes observed in the first form, become afterwards replaced by greyish or slate-colour spots (Atlas, Plate VI., Fig. 6); in other words, they undergo fatty degeneration.

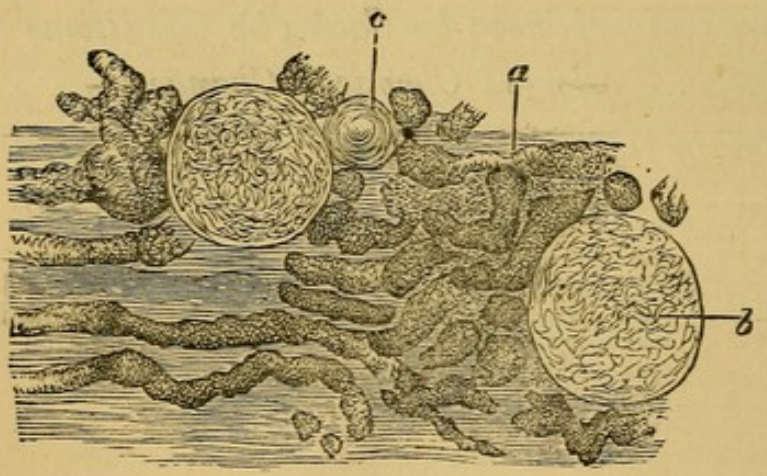

FIG. 13.—SECTION OF KIDNEY IN A CASE OF BRIGHT'S DISEASE, ARRIVED AT THE PERIOD OF FATTY DEGENERATION.
a Opaque Uriniferous Tubes; *b* Normal Glomerulus; *c* Section of an Arteriole likewise healthy. Magnified 70 diameters.—*(After Cornil.)*

The renal veins *are thickened*, and present fibrinous concretions adherent to their walls, which occupy their principal ramifications. In those cases the cortical substance appears more humid on section, as in those where that disposition of the veins does not exist. The lymphatic ganglia of the pelvis of the kidney are sometimes enlarged, but this is rare.

Again, the calyces and pelvis sometimes present traces of inflammation in the acute form, and vascular

arborizations; in the *chronic* state a white or whitish-blue colour of the mucous membrane exists, and there may be ulceration. Hence, M. Litre remarks, "Let us consider for a moment the characteristics of that description (of Rayer's first form), cast our eyes over the figure which Rayer has given, and we find swelling of the organ, and that swelling often considerable. We have besides a general redness of colour indicating hyperæmia more or less general, and the cortical substance is entirely gorged with blood. If one adds to these considerations that during life pressure on the loins causes distinct pain; and if it be considered that the antiphlogistic treatment is of the most incontestable benefit in the first form, that the blood withdrawn is buffy, it will be admitted that the morbid condition of the kidney described (Rayer's first form) is a true inflammation." This Rayer himself admits, for he remarks that the analogy of cachectic nephritis with other inflammations is very striking, when their causes, their symptoms, their treatment, and especially the anatomical characters of their first and last period are regarded.

When the peculiar leisons of cachectic nephritis are complicated with diseases of the bladder, prostate, or urethra, these must be regarded as simple coincidences; but certain leisons of the heart such as hypertrophy, of the lungs, of the stomach, and of the intestines, are sometimes primary, sometimes secondary affections.

Cachectic Nephritis a blood Disease.—Evidences: It is frequently associated with similar degeneration in the structure of other glands, such as the liver, spleen, and pancreas, &c. Both kidneys are usually affected. In his extensive experience Rayer never saw the affection

unilateral. I have, however, seen one, consequent on scarlatina, a large mottled kidney existing on the one side, the other being perfectly healthy. It exists coincidently with other abnormal states of the system, with most of which its manifestations are pathologically reconcilable.

Condition of the Blood in Cachectic Nephritis.—To Christison we are mainly indebted for our knowledge of the condition of the blood in cachectic nephritis. In proportion as the albumen escapes from the blood the density of the serum is diminished: from 1029 to 1031 or even 1819, and the solid matters are reduced from 100 to 102 in a thousand, to 68, 64, or even 61.

The amount of fibrine is, on the other hand, increased. In healthy blood it exists, according to Dr. Christison's calculation, in the proportion of 25 to 52 parts in a thousand; but in the acute stage of nephritis he has seen it as high as 82; he has seen it however, as low as 30, and considers the variation, to be due to the degree of local inflammation. Generally speaking, the proportion of fibrine is increased, and I believe, as we shall see in the sequel, that the amount of fibrine has an intimate relationship with the proportion of urea eliminated.

As the disease advances the density of the serum and the proportion of solid constituents may even exceed that of health. When there is but little coagulability of the urine, and consequently but little albumen in it, the density of the serum may amount to 1030; and while the normal proportion of salts and albumen to the entire blood, according to Lecanu, is 800, and to Christison, 816 to 853, it may now be as high as 970. The fibrine is usually in normal proportion in the blood,

after the acute stage is passed, and becomes abundant only when reaction sets in.

Coincident with the further progress of the malady, there is a decided diminution of the red globules of the blood, and with them are seen other globules of a whiter colour and of a larger size than they. Is it not possible that these globules may have some connection with Dr. Johnson's exudation cells?

Urea* as already remarked, was first shown to exist in the blood in Bright's diseases by Bostock, and not by Christison, as Johnson remarks. The fact was verified however, by Christison in 1829, and after that by Wilson, in 1833 *(London Medical Gazette)*. Dr. Owen Rees confirmed these observations.†

Period of Life at which Bright's Disease most frequently occurs.—Acute Nephritis may occur at any period of life, but cachectic nephritis is most frequently met with after middle life, and in persons, as a rule, who take little exercise and live freely. In general terms the different stages of disorganisation of the kidney, may be classified as the stage of hyperæmia, the stage of exudation and its consequences, and the stage of contraction or atrophy.

Supposing a person to die during the stage of inflammatory congestion of the kidney, though this is somewhat a rare occurrence, basing upon analogy we would expect to find a condition similar to that which would

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* M. Marchand ("De l'Existence de l'Urée," &c,, t. ii., p. 43) showed, by the following operation, that urea is simply eliminated by the kidney: In a sheep he tied the vessels and nerves of the kidney in one ligature; the animal was killed two days afterwards, and 400 grammes of blood gave two grammes of urea: 60 grammes of the contents of the stomach gave 2 grammes of urea.

† *London Medical Gazette*, vol. xii.. p. 976. *Ibid.* Bret and Bird. Also Nysten, *Journal de Chimie Medicale*, 2iéme Series, vol. xii., p. 257.

be found in a case of acute pneumonia or meningitis. This is exactly what obtains, and the appearance of such a kidney is admirably represented in Bright's fifth plate. The following is Bright's own description: The kidneys presented a very curious appearance; they were easily slipped out of the investing membrane, were large and less firm than they often are, of the darkest chocolate colour, interspersed with a few white points and a great number nearly black, and this with a little tinge of red in parts gave the appearance of a polished fine-grained porphyry, or greenstone. On cutting longitudinally into the kidney, this structure and these colours were found to pervade the whole cortical part; but the natural striated appearance was not lost, and the external part of each mass of tubuli was peculiarly dark;—the whole mammillary processes were of a dark colour. On being cut through and left for some time, a very considerable quantity of blood oozed from the kidney, showing a most unusual accumulation in the organ; and indeed it seemed to be from this cause that the peculiar appearance and colour arose, the very dark spots being the effect of blood either extravasated or in vessels greatly gorged. We next examined, Bright continues, the epiglottis, and this was found to be thickened by an œdematous effusion beneath the membrane on its upper side; it was bent into the form of a pent-house with a sharp angle; and the lower surface was also thickened, and presented a doubtful appearance of superficial ulceration. Patient died from œdema of the glottis. This was a decidedly acute case. The day before the attack, about ten days before his admission into Guy's Hospital, he had been employed in washing skins; his feet were very wet; he found the swelling

coming on about six o'clock the same evening, and he continued to swell until coming into the hospital, on the 15th November. At that time he was labouring under general anasarca, and the urine was scanty, and on the 19th coagulated by heat. The urine at intervals contained albumen and blood. The patient died on the 5th December (the month following) from symptoms of suffocation.

Compare with Bright's case the following case: this kidney is exactly similar in appearance to that depicted by Bright, and the history is almost analogous:—

Joseph Henderson was admitted into the Royal Infirmary of Glasgow, December 2, 1873, complaining of swelling of the face, body, and lower extremities, of *one week's* duration. Of late he has often been wet, and frequently slept in his wet clothes: as he had no home, he had no opportunity of changing his clothes. He frequently got drunk. The cutaneous surface is pale, and the features are swollen; eyelids œdematous, and patient states that the swelling began in the eyelids. He thinks he passed as much water since the illness began as he did in health. *Great pain* was felt in the lumbar region. Tongue dry and coated; bowels confined; pulse 90; temperature 105°; and skin dry. The abdomen is enlarged, and there is well-marked fluctuation. Pitting, on pressure, is well-marked nearly all over the body. Heart sounds are weak and indistinct, with a ventricular systolic murmur, best heard over apex. The urine is of a light amber colour; specific gravity, 1020; abundant precipitate of albumen with nitric acid and Tidy's test. Epithelial casts were found in abundance, and the urine contained blood. Patient died December 15th. The kidney, you will observe, is con-

siderably enlarged; weight 8 ozs. The cortex presents a dark and highly congested appearance, with interspersed patches of ecchymosis. The capsule peels readily off; and on section you see that the cortical substance is thickened and loaded with dark fluid blood. The medullary portion of the kidney is likewise congested.

The statement of the patient that he made as much water as in health I regard as unreliable; and the high specific gravity of the urine was due to the presence of abundance of lithates. At the risk of a little recapitulation, let me return to the fact that the changes produced on the kidney are upon one or all of three structures—viz., the basement structure of the kidney, the secretory structure, or the vascular structure; and while these usually involve all three, they also present four pathological varieties: they may consist of the nature of hypertrophy, atrophy, degeneration, and the appearances due to exudation. We have seen how the cortical substance and its prolongations inwards—the septula renum—enlarge from congestion, and by thus compressing the tubular structure between it and the engorged Malpighian tufts, cause it to exhibit a duller colour, and render its striæ less apparent than in health; or the cortical substance and its prolongations may become sodden by effused albuminous products due to impeded circulation. This condition is apparent in Rayer's first variety—"Cet état induré du rein est la dernier dégré du travail morbid dont l'hypérémie rénale *est le debut.*"

The hyperæmia and anæmia are sufficiently explained by derangement of the circulation, due to fibrinous concretions.

If the inflammation be sufficiently intense blood serum is effused, and this we recognise as the whitish

or ashy product consisting either of solitary and accumulated molecules, or of fibrinous coagula and pus corpuscles (Gluge), which may be deposited in any part of the renal parenchyma external to the blood vessels, but which is more particularly found in the Malpighian corpuscles, giving rise to the condition designated by Bright, "granular degeneration of the kidney." *This* granular degeneration must be distinguished from that arising from simple granulations of lymph interspersed throughout the kidney, and of a yellowish appearance.

But if the glandular epithelium of the convoluted tubes be shed, in proportion to the extent of this so will contraction or atrophy of the organ ensue; and this may be due to the contraction of fibrinous bands in the connective tissue, or mere collapse, as it were; and if fatty degeneration either of the secretory cells, the basement structure of the kidney, or the walls of the vessels, takes place, there exists the sixth form of Rayer, that figured in Bright's third plate, or Johnson's "granular fat kidney;" and if the blood-vessels be affected, the so-called "lardaceous

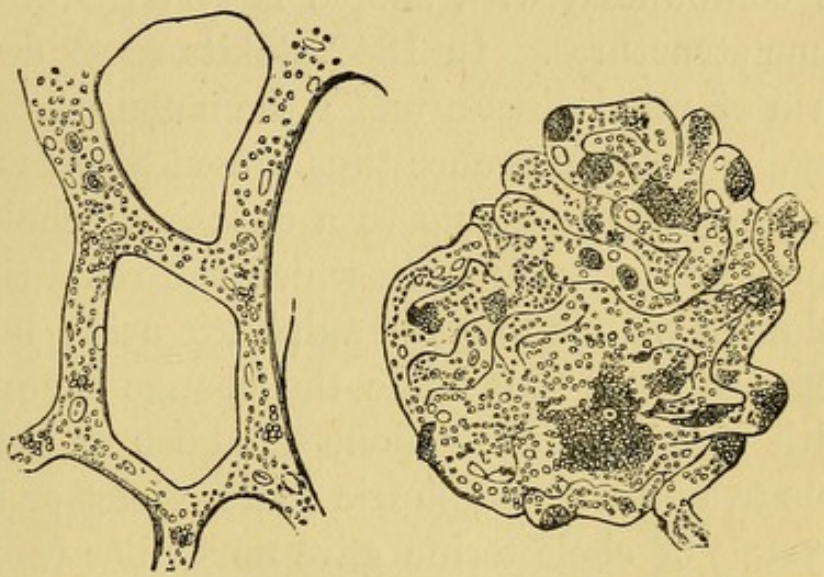

FIG. 14.—FATTY DEGENERATION OF THE BLOOD—VESSELS OF THE KIDNEY IN A CASE OF BRIGHT'S DISEASE.

On the left hand side is represented Fatty Degeneration of Capillaries and of the Stroma of the Kidney; on the opposite side, the Vessels of a Malpighian Capsule in a state of similar degeneration.—*(After Cornil.)*

kidney" is the result. The latter phenomenon is usually coincident with scrofula, syphilis, prolonged suppuration, &c. The diseased action is primarily on the vessels: the connective tissue and parenchymatous structure is only secondarily involved. If the fatty degeneration be general throughout the entire organ, we have the form admirably displayed in Bright's fourth plate, "the large white kidney," or "simple fat kidney" of Johnson.

The *lardaceous* change in the blood-vessels must not be confounded with simple fatty degeneration of the same structures. In 1842 Rokitansky* described this form of renal disease under the name "lardaceous kidney." The appearance thus presented was regarded by Meckel† as being due to a deposit of cholesterine, because of the manner in which the renal tissue became coloured with iodine and sulphuric acid; but Virchow‡ demonstrated, that while the change in question gave with iodine solution alone a reddish or reddish brown colour, and with sulphuric acid a violet or blue colour, crystals of cholesterine gave no similar result on being treated with iodine alone; and, on the other hand, sulphuric acid alone gave a reddish brown coloration. In view of this reaction, Virchow regarded this form of degeneration as being of a similar composition with vegetable starch, and accordingly named it amyloid. Elementary analyses of this material by Kékulé and Schmidt,‖ and Rudneff,** showed that instead

* Lehrbuch der Patholog. Anat., t. II., p. 429. 1842.

† Annalen des Charite Krankenhauses. 1853.

‡ Archiv. für Pathol. Anat., t. VI. et VIII.

‖ Verhandlungen des Naturist-Med. Vereins zu Heidelberg. 1855.

** Annalen der Chémie und Pharmacie, LX., p. 250. 1859. These analyses are confirmed by M. M. Charcot and Berthelot (*Journal de Physiologie* of Brown-Séquard, t. II. 1859.)

of being a hydrate of carbon, and destitute of nitrogen, it was, on the contrary, an albuminoid compound. There is no objection, however, to the retention of the term amyloid, if it be simply regarded as expressing an appearance, and not necessarily indicating a definite chemical composition.

Lardaceous degeneration of the kidney is usually associated with a changed condition of the cells of the convoluted tubes. There exists parenchymatous nephritis, *plus* lardaceous degeneration of the blood-vessels. This alteration usually begins in the Malphigian capsules, which become thus larger, more transparent, and more refracting than in the normal state. Ultimately the vessels of the glomerulus, and the arterioles and capillaries become affected; and their calibre is so diminished by thickening of their walls that the most penetrating injections cannot be received. On microscopic examination they are found to have become transparent, their cells and fibres are less apparent than in health; and they are embedded in, and swollen by a finely granular matter. In treating them with a simple solution of iodine, or, to obtain a deeper colour, with the addition of a few crystals of iodide of potassium, the vessels become brown, or reddish brown, while the other structure of the kidney remains of a yellow colour. The preparation being then covered with a piece of thin glass, superfluous water being pressed out, and treated with a drop of sulphuric acid, the following results are obtained:—Most frequently the brown colour assumes a deeper tint; but in other cases a succession of colours is the result, the brown parts passing successively through a deep green, and an indigo blue, finally to violet and red. The walls of the uriniferous tubes

and the epithelial cellules are not affected with the amyloid change,* save in some exceptional cases of long duration.

Significance of Tube Casts.—It has been long taught, and the statement has been repeated in the most recent writings on this subject, that the basis material of tube casts is fibrine. This opinion, however, if we follow the analysis of Rovida,† must now be abandoned. According to the investigations of this authority, hyaline casts are composed of an amorphous substance, differing in chemical composition from fibrine and chondrine, and rather approaching to that of gelatine. Their physical characteristics are as follow:—They are colourless, flexible, and possess little refracting property. Sometimes on the surface of these tubes, and at other times occupying their interior, white and red blood-corpuscles may be found, as likewise the nuclei of cells, the cells themselves, and fat globules. To the extent that the latter elements are absent, the hyaline condition is more manifest, and *vice versa*.

The material of which these casts are composed may be derived from the glomerulus, or the surfaces of

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* Rosenstein has tabulated the extent to which the amyloid renal change existed concomitantly with certain diseases, and presumably dependent thereon, in the following manner, collecting the cases published by Wagner, Méckel, Virchow, Traube, Robin, and Guigon :—

In 100 Cases of Amyloid Kidney Disease—

1.	Pulmonary Phthisis existed	in 44
	In combination with Suppuration of Bone,	,, 46
	With Syphilis,	,, 1
2.	Osseous Suppuration,	,, 29
3.	Syphilis,	,, 15
4.	Empyema,	,, 3
5.	Carcinoma,	,, 3
6.	Psoas Abscess,	,, 2
7.	Pyelitis and Hydronephrosis,	,, 2
8.	Abscess of the Liver,	,, 1
9.	Chronic Alcoholism,	,, 1

† Centralblatt, 1872.

the tubes themselves; and it will be obvious that the larger the mould in which they are formed, in relative proportion will be the size of the casts; hence large tubes indicate formation in urinary canals divested of epithelium, while small ones indicate the integrity of the cell lining. But yet another inference is to be deduced from the relative size of the urinary canals of the kidney — the descending *branch of the loop of Henle is so small that it is extremely improbable that casts formed in the convoluted tubes* are ever found in the urine; and consequently, so far as the morbid condition of the cortical substance of the kidney is concerned, the presence of tube casts in the urine has been accorded a clinical importance which, strictly speaking, it fails to merit. On *post mortem* examination, cylinders are *never* found within the glomerulus; they are found in the convoluted tubes, especially in parenchymatous nephritis, as obstructive clots, hyaline in the centre, and granular on their circumference.

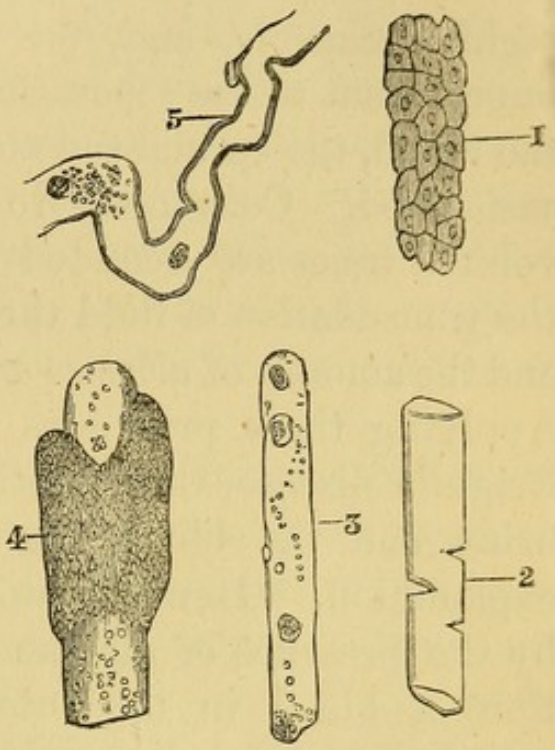

FIG. 15.—HYALINE CYLINDERS IN A CASE OF ALBUMINOUS NEPHRITIS.

1 Desquamated Renal Cells; 2 Hyaline Cylinder with jagged edges; 3 Hyaline Cylinder with fragments of cells adhering, and occasioning a granular appearance; 4 Hyaline Cylinder covered with fatty granulations; 5 Hyaline Tube, of which the smaller portion seems to correspond to the *intermediate, or canal of union.*

To this condition my friend Professor Béhier has applied the term endartérite oblitérante; which, if it be

of an aggravated nature, constitutes the condition designated by Dr. Johnson the "cloudy swelling." In a direct ratio to the intensity of this condition there will exist, on the one hand, a *mechanical* obstruction to the transudation of fluid through the Malpighian capsule, and, on the other, a *physiological* impediment to the separation of the urinary salts from the blood, the special function of the gland cells being suspended. Conversely to the extent that the convoluted tubes are denuded of their gland cells, so is the transudation of fluid through the gland facilitated, and the amount of *albumen and salts in the blood increased.* Applying these principles to the particular forms of Bright's disease, the variations which the state of the urine and the blood present admit of a scientific explanation. Hence acute nephritis is characterised by the presence of albumen in the urine, the circulation of blood in the intertubular capillaries being retarded, as already explained; hence the frequent admixture of blood with the urine, the rapid development of anasarca, and the effusions into the peritoneum, the pleura, and the pericardium. And with regard to the urine itself, it is voided with pain, is diminished in quantity, generally much below the specific gravity of health, and is often but slightly acid, or even alkaline. In the "small red granular" kidney dropsy is *not* a common symptom. And why? Because large hyaline and granular casts are frequently found in the urine in these cases, the urine is often *in excess* of the quantity secreted in health, and the specific gravity is *reduced* as low as 1010 to 1005; and the diminished specific gravity is mainly due to the absence of urea, uric acid, and extractive matter. In

one of Dr. Christison's cases the total amount of solids discharged with the urine was reduced to a fifth, and in another to one-twelfth of the healthy average. In the "large white kidney," on the other hand, dropsy is one of the most frequent symptoms. In twenty-six cases of this variety Dr. Johnson observed this symptom in twenty-four. This is doubtless due to the pressure exerted on the intertubular capillaries by the enlarged tubes which are characteristic of this variety. The epithelium of the convoluted tubes is likewise unusually opaque and bulky, and, as already referred to, the proportion of albumen and salts in the blood is very high.

Reverting still further to the clinical significance of tube casts, it is to be noted that their most frequent seat of formation is the loop of Henle, and the particular portion of it, the ascending branch. They are also found in the collector canals, and in the *intermediate* portion of the kidney; and, as already remarked, vary in size according to the particular canals in which they are formed.

Tube casts are found in the *region of the straight tubes* under the following circumstances:—1st, *Hyaline* tube casts may be found in the urine in health, according to Klebs, Axel Key, Robin (1855), Rosenstein, and others; and in obedience to the law postulated in the first lecture, as you may remember, relating to the influence of depraved blood on glandular structure, tube casts have been frequently* found in the urine in aggravated cases of jaundice. It is clear that the biliary acids in the passing through the kidney deter-

* Nothnagel (Deutsche Archiv., 1873, p. 326).

mine such an amount of inflammatory irritation as to cause the formation of casts, for conformably Leyden has observed them in the urine of animals into whose blood biliary acids had been injected. *Epithelial cylinders* are in like manner common enough during the active stages of fever, and following the administration of strong diuretics. 2nd, Casts are found in the urine of animals which have been covered with varnish, and thus rendered albuminuric. 3rd, In the diverse forms of Bright's disease, as already seen. And 4th, In cases of phosphorus poisoning, or *phosphoric steatose.* Ranvier, in these cases, has found them to a small extent in the straight tubes, but in an especial manner in the loop of Henle.

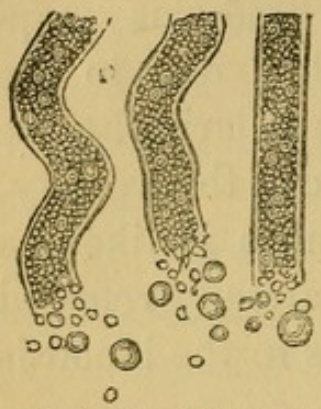

FIG. 16.—FATTY DEGENERATION OF TUBES FROM THE CORTICAL PORTION OF THE KIDNEY IN A CASE OF PHOSPHORUS POISONING (PHOSPHORIC STEATOSE.)—*(Ranvier.)*

Varieties of Tube Casts.—In addition to the hyaline tube casts already referred to, the following modifications may exist, and indicate special degenerations. The peculiar characteristics may be due, 1st, To gland cells. If tubes having thus a granular appearance have existed a long time in the urine, their presence may be taken as indicating a chronic lesion of the kidney, usually interstitial nephritis. It is necessary to distinguish these granular cylinders from the *granulo-fatty* cylinders described by Ranvier as existing in cases of poisoning by phosphorus: 2nd, Blood corpuscles may be found imbedded in the basis material of the tubes: 3rd, Fat cells: 4th, Exduation cells: and 5th, The tubes may be of a waxy nature, more brittle, and with edges more or less jagged. These tubes are easily

coloured by carmin, and especially iodine, which imparts to them a yellow-brownish coloration.

Even as the occasional presence of sugar in urine must not be regarded as constituting diabetes, and justifying a serious prognosis, so care must be taken that the occasional presence of hyaline tube casts in the urine be not accorded an exaggerated significance; as with sugar in diabetes, it is their *persistent* and *abundant* presence in the urine that indicates renal structural changes. Finally, you must guard against another source of error: cases of Bright's disease exist in which no tube casts are found in the urine. This happened in a case of parenchymatous nephritis observed by Ackermann.* In these cases the tubes are found after death retained in the pelvis of the kidney, and with or without other adventitious matter.

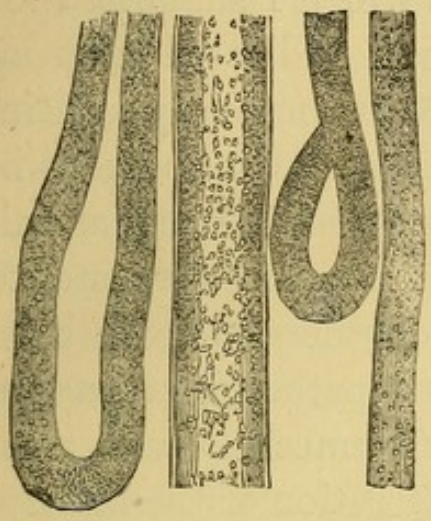

FIG. 17.—LONGITUDINAL SECTION OF THE TUBULAR SUBSTANCE OF THE KIDNEY IN A CASE OF ALBUMINOUS NEPHRITIS DUE TO POISONING BY PHOSPHORUS.

The Loops of Henle are more altered than the straight tube between them.

Causes of Cachectic Nephritis.—The causes of Bright's disease may be thus classified: 1st. Poisons eliminated by the kidney, and foreign to the composition of the body. 2nd. Blood disorder occasioning constitutional disease, whereby unhealthy blood is presented to the kidney, and structural changes consequently ensue (*vide* page 13). These embrace scarlatina, typhus, alcoholism, gout, rheumatism, scrofula, syphilis, phosphorus, lead, and arsenic poisoning, phthisis, typhoid fever, diphtheria,

* Centralblatt. (1872, p. 606.)

malassimilation due to over-eating, and Rayer includes Onanism.

The limits of these remarks forbid a detailed examination of all these causes as producing cachectic nephritis: but there is one—viz., chronic alcoholism, which has such a direct influence on this disease that its discussion is imperative.

In a classification* of diseases which I submitted for consideration not very long ago, I indicated that an important group of diseases were immediately contingent on deficient oxidation of tissue. Conspicuous in this group I placed gout, rheumatism, neuralgia, calculous diseases, diabetes, &c.† I am now disposed to add fatty degeneration. Fatty degeneration, we have seen, plays, so to speak, a prominent pathological part in cachectic nephritis. What is its connection with alcoholism? In discussing fatty degeneration of the kidney, Dr. George Johnson remarks: "Fat kidneys are common in the domestic dog and cat, probably because these animals lead indolent lives, and consume large quantities of food rich in hydrocarbons. These animals are the counterpart of the human animal when, from eating and drinking to excess, he grows fat, and gets fat liver, heart, and kidney. The unhappy Strasburg geese afford an illustration of the fatty infiltration of the liver resulting from a wasting disease. In order to obtain fat livers for patties the animals are well fed and fattened; then they are confined in heated cages without food and water. They become feverish, and rapidly

* Author's "Observations on Therapeutics and Disease" (Churchill).

† The views in question, I may here remark, were then (in 1870) considered *outré* by reviewers. Since that time, I have had the satisfaction of noticing that they have been followed up by Dr. Murchison, in his able Croonian Lectures, recently delivered, and by other writers.

waste, while their livers grow large. It seems probable, as Baron Larrey long ago suggested, that the oil absorbed from the adipose tissue enters the circulation and infiltrates the cells of the liver, and probably in a less degree of the kidney also." I certainly do not regard this as the correct explanation ; it does not explain the formation of the oil, and it requires two gratuitous hypotheses to support it. I offer the following explanation :—

It is from the textures of the body, by a process of oxidation that all the excreta, directly or indirectly, are formed. If the blood contain too great an abundance of nutritive pabulum (*vide* p. 13) relatively to the destruction of tissue, two results may happen—1st. If this pabulum exist, *e.g.*, in the form of protein, the nitrogen and sulphur being removed, suppose for the formation of taurin (C_2 H_7 NO_3 S), the remaining portion may be *deposited* in the form of fat (Oleine, C_{39} H_{36} O_5) ; but 2nd, It happens that the blood must contain too little oxygen (and here indolent lives and food rich in hydrocarbons *do* play an important part) with respect to the tissues to be reduced, and instead of fully oxidised* excreta being the result, *intermediate* compounds are formed, which, on the one hand, may constitute the *materies morbi* of certain diseases. To this class belongs, undoubtedly, fatty degeneration.

Observe that fibrine of muscle is represented by the following formula—C_{216} N_{27} S_2 H_{169} O_{68}—same as blood albumen. It contains the elements for the formation of uric acid (C_5 H_4 N_4 O_3), urea (CH_4 N_2 O), the bile acids —glycocholic acid (C_{26} H_{43} NO_6), taurocholic acid

* Author's Pamphlet, "On Therapeutics and Disease."

(C_{26} H_{45} NO_7 S). All the sulphur of the bile is contained in the latter. Supposing, then, the oxygen contained in the blood to be insufficient to effect the normal chemical change, the oxygen may unite with the sulphur to form sulphuric acid, a part of the nitrogen would go to form ammonia, and the recombination of carbon, hydrogen, and oxygen with the remainder of the nitrogen would result in the formation of intermediate compounds, such as fat, leucin (C_6 H_{13} NO_2), and tyrosin (C_9 H_{11} NO_3), which are merely products proceeding to higher oxidation.

Fat would thus be not *deposited*, but *formed;* and that this is the case is indicated by the fact that fatty degeneration of muscles takes place *within* the sarcolemma, and of cells *within* the cell-wall. Fats are a combination of fatty acids with a hypothetical radical termed lipyle, with which they form respectively *oleine* and *margarine.* Thus, lipyle C_3 H_2 O + oleic acid C_{36} H_{34} O_4 = C_{39} H_{36} O_5 one atom of oleine; or with one atom of margaric acid one atom margarine is formed—thus, C_3 H_2 O + C_{34} H_{34} O_4 = C_{37} H_{35} O_5. Given thus, certain circumstances that cause an excess of carbon in the blood, relative, or actual, the oxygen becomes inadequate for the conversion of tissue, is probably seized by the effete elements circulating in the blood, and fatty degeneration as one of the results ensues. I assume that alcoholic indulgence is admitted to exercise a direct influence on the causation of Bright's disease. In twenty cases of cirrhosis of the kidney, Dr. Grainger Stewart noted that twelve occurred in intemperate individuals. Alcohol, then, being a hydrocarbon, appropriates the oxygen which should have effected the reduction of tissue, renders the blood thus impure, and

brings about in consequence disorganisation of secretory structures as indicated.

This accords, as we have seen, with the period of life at which cachectic nephritis occurs, and the class of individuals in whom it is found.

Conformably still further with these opinions, it is to be noted that in the first place alcohol, given as it properly is in certain cases of fever,* diminishes the temperature. Its primary effect is that of a cardiac stimulant; hence the exhilaration: its secondary effect is that of a narcotic; hence the depression. With this condition there is not unfrequently associated a feeling of warmth of skin. This is due to a dilatation of the cutaneous capillaries, the sympathetic fibres being more or less paralysed. The capillaries of the brain are similarly influenced; and it is at this stage, and not in the primary, that I believe apoplexy from alcoholism is most prone to occur. The exhalation of carbonic acid gas from the lungs is notably diminished by the exhibition† of alcohol, and owing to the same cause,‡ the urine contains an abnormal amount of uric acid, and the quantity of urea is correspondingly diminished.

In a paper read to the Royal Medical and Chirurgical Society§ Dr. Dickinson arrived at the following conclusions on this subject: "Alcohol causes fatty infiltration and fibroid encroachment; it engenders tubercle, encourages suppuration, and retards healing; it produces untimely atheroma, invites hæmorrhage, and anticipates age. The most constant fatty change, replacement by

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* *Vide* Author's "Observations on Therapeutics and Disease."

† Perrin, Lancereaux, Dictionaire Encyclopédique des Sciences Médicales (Alcoolisme)—Râcle, De l' Alcoolisme Thèse pour l'agrégation.

‡ Author's Op. Cit.

§ *Lancet*, Nov. 2nd, 1872.

oil of the material of epithelial cells and muscular fibres, though probably nearly universal, is most noticeable in the liver, the heart, and the kidney. The fibroid increase occurs about the vascular channels and superficial investments of the viscera, where it causes atrophy, cirrhosis, and granulation."

According to Magnus Huss fatty granulations are usually present in the blood of inebriates; and Lallemand, Perrin, and Duroy hold that these granulations are composed of tiny crystals of cholesterin (C_{26} H_{44} O) —a fatty substance—and oil globules. Cholesterin is probably one of the intermediate compounds formed in the liver, when the function of the organ is impaired. These observations are confirmed by Gallard, of Paris, in his "Leçons Clinique Medicale." The blood thus altered seems to exercise a particular action on the several glands. In the case of the *vena portæ* it sets up adhesive phlebitis, an arrest of the circulation consequently supervenes, and the intimate structure of the liver becomes ultimately affected. Further, the presence of alcohol in the parenchyma of the liver exercises an influence over the glycogenic secretion, *which becomes more active*, and congestion is produced, manifesting itself in pain and enlargement of the organ.

What of the Strasburg goose?* It is confined in a dark, heated place; motion is denied it; food is actually mechanically pressed down its gullet. What are the results? It breathes an atmosphere surcharged with carbonic acid on account of its proximity to the fire; it respires less air owing to its restricted motion, and the dispro-

* "On deplume l'estomac de oies; on attache ensuite ces animaux aux chenets d'une cheminée, et on les nourrit devant le feu. La captivité et chaleur donnent a ces volatiles une maladie hepatique qui fait gonffer leur foie."—(Cours Gastronomique.)

portion between the diminished quantity of oxygen in the blood and food is still further increased by the forced surfeit, and fatty degeneration necessarily ensues in the manner indicated.

Purulent Degeneration.—To the formation of pus, as above observed, certain of the pathological features of cachectic nephritis are due. This is, however, more characteristic of simple nephritis. Purulent degeneration is closely allied to that form of tissue change which we have just dismissed. Fat is one of the products of imperfect metamorphosis of tissue element; so likewise is pus. Let me remind you of the physiological conditions that lead to the pathological ones, of which pus is a manifestation. When a healthy part is artificially irritated, contraction of the minute capillaries ensues, accompanied with pallor due to diminution of the quantity of blood, though the current is quickened according to the hydraulic principle, that when a certain quantity of fluid is driven through a tube with a certain force, and the calibre of the tube diminished, the force remaining the same, the current is quickened in a direct ratio. After a short interval nervous exhaustion supervenes, and the minute blood-vessels become, in consequence, preternaturally dilated; and the course of the blood is retarded, though its quantity is increased. If the irritation have been sufficiently intense, ulterior states may supervene; a particular oscillation of the blood takes place in the capillaries, and it ultimately becomes entirely arrested, liquor sanguinis is effused into the surrounding tissues, and concurrently the classic inflammatory symptoms of heat, swelling, and pain become developed. The part is now *partially* dead: if wholly dead, mortification would be the result.

As it is, a compromise, so to speak, is effected—*i.e.*, the nucleated lymph cells destined to repair the waste of tissue not being appropriated, owing to the interference with the circulation, and the arrested transformation of tissue, degenerate into pus cells. The white corpuscles of the blood also contribute, through a similar degeneration, to the totality of pus cells. Since the publication of my pamphlet "On Therapeutics and Disease" (1870), to which I have already referred you more than once, and in which I enunciated these opinions, Hoppe-Seyler has obtained results of a confirmatory nature.* He introduced fresh crystalline lenses into the abdominal cavity of dogs, and analysed them after a period varying from one to fourteen days. The lenses became infiltrated with lymph corpuscles. Glycogen—and you will note the important relation of this fact to what will be brought under your notice in the following section—was found in greatest abundance at the eighth day, at which period the lenses contained the greatest number of contractile corpuscles. The glycogen is the product of these corpuscles. If the lenses were not plunged immediately into boiling water, but allowed to stand for some time, *no glycogen was found, but in its place sugar.* In the pus of congestion-abscesses no glycogen occurred. When glycogen is found, it is observed to co-exist with, and to depend upon, the lymph corpuscles; when the purulent transformation is complete the glycogen disappears.

Increase of Urea in the Blood in Cachectic Nephritis.—At the outset of our examination of this point, the question presents itself, Is the increase of urea in the blood simply the result of diminished elimination or

* Med. Chem. Untersuch. 1871.

increased formation? and has the increase of fibrine in the blood any relation thereto? You will remember that I regard the special function of the secretory cells of the convoluted tubes to be that of separating the saline constituents of the urine; and that to the extent that these cells are removed by desquamation so is the amount of urea in the blood increased. I believe, as I shall endeavour to show presently, that in cases of cachectic nephritis *less* urea is formed than in health, and that this accounts for the *increase* of fibrine in the blood, *particularly in the acute stages, and when reaction ensues.* The chemical changes that are effected in the liver are due to oxidation, and oxidising processes are, as you are aware, always accompanied with the evolution of more or less heat. Hence, while the average temperature of the body is between 90° and 99° Fahr., the temperature of the healthy liver reaches 104°, or even 106°; and Bernard has shown that in dogs the blood in the hepatic veins is considerably higher than that in the portal vein. The grounds on which the belief in the formation of urea by the liver is based are the following: Meissner found it in considerable quantity in the livers of mammalia; and in certain forms of hepatic disease the amount of urea in the urine is notably diminished. Popp* states that urea is a constant constituent of bile; and according to him the bile of the pig contains it in larger quantity than that of the ox. Ritter† confirms the observation of Bechamp, that urea may be obtained from *albumen, fibrine, and gelatine*, by oxidising them with potassium permanganate.

* Zeitschr. für Chem. (2) vii., p. 88.
† Comp. Rend. lxxiii. 1219.

Rose* long ago stated, that after repeated observation he found a diminution of urea in the urine in cases of acute and chronic hepatitis. This was confirmed by Dr. Henry, of Manchester, and afterwards by Prevost and Dumas,† Berzelius, and others. Vogel records a case of cancer of the liver in which scarcely a fourth of the normal quantity of urea was found in the urine.

Frerichs, in a case of acute atrophy of the liver, found no trace of urea in the urine, *but instead leucin and tyrosin.* More recently Cyon performed the following experiment, which confirms this view: The whole of the blood was extracted from the carotid of a dog, and a portion, after being defibrinated, was transmitted by means of mercurial pressure through the liver; coincidently a canula was introduced respectively into the vena cava inferior and the hepatic artery, and the vena portæ, and the results were found to be, that blood which had passed through the liver contained a much larger proportion of urea than ordinary blood. In one experiment 100 cubic centimetres of the arterial blood, when defibrinated, contained 0·08 grammes of urea; but after having been passed four times through the liver, the same quantity contained 0·176 grammes.

Again, the liver produces a compound termed glycogen ($C_6 H_{10} O_5$). The formation of glycogen in the liver is augmented by an amylaceous diet, but the liver can form it from peptones without the intervention of amylaceous or saccharine articles of diet. Glycogen constitutes an intermediate link between azotised products and sugar. Thus Bernard remarks, "The for-

* Biblioth. Med., t. lvii., p. 12.

† Annales de Chimie, t. xxxiiii., p. 201.

mation of sugar (in the liver) is, in fact, only the beginning of a series of phenomena of combustion, which ultimately result in carbonic acid. When the vital energy decreases the sugar diminishes in the blood and the liver, the same as the carbonic acid in the expiration." Observations on hybernating animals prove the same thing. The temperature of the animal, the rapidity of the circulation and respiration are lowered: it is the same with glycogenesis. If the liver of a frog plunged in the hybernal sleep be examined, no sugar is found, but only glycogenic matter. When the animal awakes and moves about sugar reappears. Hence, the less complete the oxidation the greater the quantity of glycogen. The value of Gallard's observation will now be understood. Alcohol exercises an influence over the glycogenic secretion, *which becomes more active.* Why so? Simply because alcohol has the same effect on oxidation as hybernation has. It is, as we have seen, a hydrocarbon, and to the extent that it is indulged in it *diminishes the amount of oxygen relatively* to the purposes to be performed. Hence it causes congestion, pain, and enlargement of the liver, ending in structural disorganisation. Furthermore, fibrine and albumen almost entirely vanish in the liver, and the bile contains so little nitrogen that it need hardly be taken into account. But if it be assumed, as there are the best reasons for doing, that urea is formed in the liver, and that fibrine and albumen disappear in it, then one element of urea, viz., nitrogen, is set free, and its union with one of *the lower products of oxidation* would form urea. With which of the lower products of oxidation would it thus unite? I think with leucin ($C_6 H_{13} NO_2$) and tyrosin ($C_9 H_{11} NO_3$). This would explain why the amount of urea excreted is

diminished by an exclusively amylaceous diet, and why the urine of the carnivora is so much richer in this material than that of the herbivora. It would further explain the views* put forth by Mr. Simon, that *fibrine is one of the constituents that have arisen from the waste of tissue;* hence the amount of fibrine in the blood is greater in *acute* nephritis—the eremacausis being more active than in the chronic; and it would harmonise with Lehmann's allegation that it is an error to suppose that arterial blood is usually richer in fibrine than venous, *the contrary being the case*, as the smaller veins contain a notably larger quantity of fibrine than the corresponding arteries.

But, again, should there exist desquamation of the secretory cells of the convoluted tubes, urea will not be eliminated except to a small extent vicariously, and its accumulation in the blood will prevent the transformation of fibrine, and the latter may thus increase in the blood from a totally different cause. In this case there is accounted for the *decreased temperature* in cases of uræmia. So constant is the decrease of temperature in uræmia that the thermometer has been used as an aid to diagnosis. It thus enables us to distinguish between hysteria, epilepsy, and uræmia. In the two former there is an increase of temperature; in the latter a marked diminution.

Not long ago M. Hanot presented to the Société de Biologie a report of an interesting case of death from

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* After the writing of the above, Mr. Alfred H. Smee, (Proced. Roy. Soc., June 16th, 1874), pointed out that when a current of oxygen gas is passed through ordinary albumen, or albumen from the fluid of spina bifida, at the temperature of the human body (98 Fah.), a certain amount of the albumen is transferred into *fibrine*. The albumen found in the urine is not capable of this transformation.

uræmic poisoning. The uræmic symptoms were primarily due to the pressure of a large carcinomatous uterus on the ureters, and mainly consisted of a kind of coma and sterterous breathing. From cerebral hæmorrhage and softening the case was diagnosed by means of the thermometer, according to the rule laid down by Bourneville. At the outset of this case the temperature was 34°, the following morning 20°, and at death only 10°.

LECTURE IV.

The Pathology of Serous Effusions in Cachectic Nephritis—Conditions that affect the Circulation of the Blood—Changes in the Composition of the Blood as a cause of Œdema—Changes in the Vascular System—Theories of their Causation—Sir William Gull and Dr. Sutton's Views—"Arterio-Capillary-Fibrosis"—Dr. Grainger Stewart's Statistics—Analogous Changes in other Organs—Affections of the Spleen and Pancreas in Cachectic Nephritis.

GENTLEMEN,—One of the earliest and most characteristic symptoms of nephritis is the occurrence of local effusions of serum—œdema—into the subcutaneous cellular tissues, particularly of the face and ankles. The immediate cause of this phenomenon may be referred—1st, *To conditions that affect the circulation of blood;* 2nd, *To changes in the composition of the blood itself.*

Conditions that affect the Circulation of the Blood.—In the normal condition of the body a constant current is in operation, between the blood on the one hand, and the surface of mucous, secretory membranes, and the tissues of the body generally, on the other. This is essential for the purposes of repair, and the removing of effete material. The amount of fluid thus parted with from the blood is very considerable—for instance, Lehmann found that, on opening the pericardium of a healthy criminal, $9\frac{1}{2}$ fluid drachms (33·8 grammes) flowed from it in $3\frac{1}{2}$ minutes—an amount equivalent in

24 hours to 488 fluid ounces. In the healthy condition both currents—the endosmotic and the exosmotic—are so balanced that the superfluous fluid is not left in the tissues, nor do the blood-vessels permit too great an abundance to flow from them. The fluid found in dropsical effusions differs from the liquor sanguinis in containing no flakes of lymph, no proliferating cells, nor pus corpuscles, as exist in inflammatory exudations. It is not coagulable on being removed from the body, and its specific gravity compared with blood serum (1029·5) is from 1008 to 1014. In order to this normal balance, free circulation of blood is indispensable, for it accords with experience as it does with hydrostatic principles, that if the circulation be retarded, blood serum transudes through the capillaries; thus, when the renal vein is tied, albumen appears in the urine.

But apart from the mechanical obstruction to the circulation of the blood there is no doubt a [illegible]logical process concerned which, in the production of the phenomenon in question, plays a most important part. We have seen that section of the splanchnic caused hyperæmia of the tubuli contorti *(vide* page 29); and Moreau has pointed out that section of the splanchnics is followed, as in cholera, by an intestinal flux. We have already inferred, it will be remembered, that in cases of acute nephritis a similar influence is caused by exposure to cold, and possibly by abnormal conditions of the blood; hence the retarded circulation and the œdema are, we assume, partially due, and in this manner, to an impeded circulation. A writer in the *British Medical Journal** remarks: "The doctrine that œdema is due to

* "Pathology of Œdema," June 15th, 1873.

venous obstruction alone rests upon a very narrow experimental basis indeed, for it is founded almost entirely on two experiments performed by Lower about the year 1680, and described by him in his *Tractatus de Corde.*" And he argues at some length as if the view that the œdema is due to an impression on the nervous system were antagonistic to the other, that which regards it as contingent on obstructed circulation. Viewed from the above stand-point, the one effect is rather the complement of the other. The immediate cause is the impression on the nervous system; then follows the retarded circulation; and it is not improbable that the structure of the capillaries partakes in a relaxation which thus affords free passage to the serous element of the blood. Conversely, stimulation of the vaso-motor nerves stimulates absorption. The experiments of Ranvier and Goltz are in perfect harmony with these views.

Changes in the composition of the Blood as a cause of Œdema.—Apart from the œdema peculiar to dropsy, the frequent occurrence of œdema in chlorosis and other leucocythæmic conditions will recur at once to everyone. In these cases the blood is literally thin, and there is a notable diminution of its red corpuscles, as in the chronic stage of Bright's disease. It is an important function of the red corpuscles to afford innervation to the nervous centres; consequently to the extent that blood is deficient in them so is there diminished nervous tone; hence languid circulation and dropsical effusion. Universal experience thus confirms the signal benefit which the administration of iron in such cases produces.

Again, in accordance with Graham's law, an influence on osmotic currents is exerted, not only by the nature of the interposing medium, but by the nature of

the composition of the fluid separated. Graham has accordingly divided substances capable of dyalisation into crystalloids and colloids. To the extent that fluid holds crystalloids in solution it is more prone to transudation. Hence, apart from the difference in the specific gravity between the fluid contained in the blood vessels and that contained in the tissues, the more the blood is surcharged with crystalloids the more prone will it be to effusion.* Dr. Murchison remarks: "There has always appeared to me to be one very important objection to this view—viz., that dropsy does not occur in that form of kidney disease in which, of all others, there is the greatest tendency to the fouling of the blood by the retention of urinary salts and urea. I refer to what is known as the contracted, granular, or gouty kidney."

On the other hand, the writer in the *British Medical Journal* already quoted is obliged to assume another hypothesis: "When it is borne in mind, also, that stimulation of the vaso-motor centres quickens absorption, and that *it is by no means improbable thut the urinary products when retained in the blood irritate them*, as they certainly do other nervous centres, we are inclined *a priori* to predict what clinical experience shows to be the case, that in the gouty kidney, where urinary products are apt to accumulate in the blood, no œdema would occur." This explanation, and the objection of Dr. Murchison, I regard as equally irrelevant. Admitting that dropsy is not of frequent occurrence in the gouty kidney, recall the pathological characteristics of the variety in question. Is it true that the solid con-

* M. Pousielle has observed in the dead subject that a solution of nitrate of potash transudes a little more rapidly than distilled water, and the same with a solution of acetate of ammonia.

stituents of the urine are eliminated by the secretory cells of the convoluted tubes, the watery by the Malpighian tufts, and that *the fluid portion of the blood would be likely to escape by the surface of the convoluted tubes to the extent that they are shed of their cloudy epithelium?* Then these are the characteristics of the gouty kidney: *large* hyaline casts are found in the urine; urine of low specific gravity is passed, usually in abundance, and there is an augmentation of salines in the blood. *Dropsy does not occur simply because the kidnegs secrete, or permit the transudation of a large quantity of urine; but no sooner do the tubes shrivel up than dropsy makes its appearance.*

Effusion may take place into any part of the body in the course of Bright's disease—into the glottis, lungs, pericardium, pleura, &c.; and in the light of what has been already stated, Rayer's statement that nephritic anasarca is more sensibly and rapidly aggravated by exposure to cold air, than any other form of anasarca, will be perfectly intelligible.

Changes in the Vascular System.—It has been already indicated that in order to healthy action there must be a normal material correlation between the blood and the tissues. When the blood presents departures from its healthy condition, the blood-vessels, in common with the other tissues, participate in the morbid action. The formation of lower forms of tissue ensues. In Bright's disease this constitutes a notable characteristic.

Dr. George Johnson claims to have discovered thickening of the arteries in this affection in 1850; but Rayer,* Bright, and succeeding writers described the same condition long antecedent to the period in ques-

* "Presque toujours il existe avec cette hypertrophie" (of the left ventricle) "d'autres lésions du cœur, des *gros vaisseaux*, ou des poumons."

tion. Hypertrophy of the left ventricle of the heart, thickening of the aorta, diseases of the arteries, thickening and inflammation of the renal veins, the existence of clots in the renal vessels, were all described by Bright, Gregory, Duncan, and Alison. Hypertrophy of the left ventricle occurred only in one-fifth of Rayer's cases, while Dr. Bright noticed it in 65 cases out of 100, and Dr. Grainger Stewart found it in 66·6 per cent., but thinks that in 8·4 per cent. other causes than renal disease contributed to the result.

In summarising 100 autopsies by Bright, 292 by Frerichs, and 104 by Rosenstein, a total of 506 examinations of cases of nephritis is given. In that number hypertrophy of the heart was observed in 177 cases. Of these 83 were complicated with valvular lesion, and 94 presented only simple hypertrophy of the left ventricle. The proportion is thus 18·57 per centum. But if the cases of advanced Bright's disease be taken into account, that is to say when the kidney had become atrophied, it is found that the per centage amounts as high as 93 per cent. (Traube).

Various theories have from time to time been propounded to account for the intimate connection thus subsisting between cases of chronic nephritis and uncomplicated hypertrophy of the left ventricle. These it will be interesting and instructive to pass in somewhat detailed review. In 1836 Bright † himself drew attention to this interesting pathological phenomenon. His explanation of it was that the altered blood produced directly on the heart an irregular excitation, or rather that it acted in such a manner on the capillaries

† Tabular View of the Morbid Appearances in 100 Cases connected with Albuminous Urine in Guy's Hospital. Reported 1836 ; p. 3, 16, et 397.

of the organism that the heart was in consequence forced to contract more energetically in order to overcome the obstacle thus caused in the capillaries. Somewhat analogous to this view was that of Christison, that the blood had been so changed that it acted on the heart as a direct stimulant, causing it to contract with increased energy, and thus inducing hypertrophy. Niemeyer remarks on this subject, "Many individuals affected with parenchymatous nephritis are affected with affections of the heart, excluding old adhesions of the heart and pericardium, as a consequence of pericarditis and valvular lesions, and of endocarditis, which is a rare affection in the course of Bright's disease. Hypertrophy of the left ventricle is thus frequently found. Traube has expressed the opinion that the hypertrophy of the heart is due to an obstruction to the passage of blood through the kidney, in consequence of which the heart acts more energetically. Bamberger and others have combated this opinion by alleging that this hypertrophy is sometimes observed in cases in which there is no derangement of the circulation. It is requisite still to collect a larger number of new observations to clear this difference of opinion. There is *always a great hypertrophy of the heart in the secondary stages of parenchymatous nephritis;* and it is certainly not alone the derangement of the circulation that is the cause of the hypertrophy in question."

M. Jaccoud thinks that the hypertrophy of the left ventricle can occur only at an advanced period of Bright's disease, and that it does not consequently occur *during* the changing condition of the renal structure. Niemeyer remarks that he has observed great hypertrophy of the heart at the commencement of the

disease; and in this he is supported by Cornil.* Grainger Stewart alleges that in the contracted form of Bright's disease in which hypertrophy of the heart existed he invariably found lesions of other organs, which might have been sufficient to give rise to the hypertrophy in question.

Traube's† view is that the obliteration of so many of the capillaries of the kidney diminishes the field of the circulation, and thus constitutes an obstruction, just as a contracted aortic orifice.

Rosenstein ranks himself among the authorities who regard the hypertrophy as being due to blood changes, an opinion which may be regarded as the English one, and to which Dr. Johnson gives his adherence.

A fact noted by Virchow somewhat confirms Traube's view. The case was one of hydronephrosis, in which the glomeruli were but a third of their normal size, and the left ventricle was considerably hypertrophied, without the existence of any other state to account for this condition.

Against the theory of blood poisoning it is contended that if this hypothesis be the proper explanation, the hypertrophy of the heart ought to take place in the early periods of the disease, a circumstance which admittedly does not accord with experience. But is this clinical fact fatal to the theory in question? And is it not possible that the hypertrophy may be due not exclusively to the one condition, but to the operation of both? To the former question I answer in the negative; to the latter in the affirmative. It is true that the hypertrophy occurs only in the advanced cases of

* Sur les Lesions Anatomiques des Reins, p. 33. 1864.
† Ueber Zussamenhang von Herz und Nieren-Krankheiten, p. 4.

Bright's disease, but it is equally true that it is then that blood poisoning begins to manifest itself. I have very recently seen, in a case of advanced tubular nephritis, hypertrophy of the heart, which came on coincidently with the progress of the disease. An undulating radial artery existed, pulmonary œdema, hœmoptysis, and unmistakeable symptoms of heightened arterial tension.

I have already insisted on the fact that between the blood and the tissues there is in health a *material correlation*—every part of the organism has its own special stimulus—and that this may be disturbed by causes interfering with the circulation, or abnormal conditions of the blood. There is an altered condition of the blood in cachectic nephritis, the urinary constituents being retained in consequence of the structural changes in the kidney. It is in the capillaries that the chemical changes of the living organism take place; and the capillaries, like cells, exhibit the properties of osmosis, capillary attraction, and chemical affinity; but in order to this occurrence in its normal state, the blood must be healthy; being unhealthy as it is in chronic nephritis these changes are interrupted, and the whole arterial system acts thus consentaneously in endeavouring to overcome the obstruction. Illustrative of this position it may be noted that Dr. Reid, long ago, pointed out that in the first stages of asphyxia the unaërated blood *passed freely through the lungs*, but was arrested in the systemic capillaries, and that the pressure in the arteries thus increased *(the hæmoptysis in advanced cachectic nephritis is very pure blood)*, while that in the veins diminished. In the second stage the converse took place, the blood became arrested in the pulmonary

capillaries, and the pressure increased in the veins and diminished in the arteries.

One possible objection to the view of blood-poisoning may be noted in conclusion. If the capillaries offer an obstruction to impure blood, would the heart not in all probability do the same? and would not the hypertrophy, instead of being limited to the left ventricle, be then general? My answer is, that the retained constituents are, so to speak, normal to the venous circulation, while they are directly toxic to the arterial system, and it is thus that the hypertrophy is limited to the left ventricle. The obstruction to the arterial circulation seems therefore to be of a twofold nature, the one relating to the kidney and mechanical, the other general, and of a physiological nature.

Sir William Gull and Dr. Sutton contend that the arterioles undergo a change to which they have applied the term "arterio-capillary-fibrosis." Their conclusions are summarised in the following propositions:—

1. The arterioles throughout the body in that condition usually called Bright's disease, with contracted kidney, are more or less altered.

2. This alteration is due to a hyaline-fibroid formation in the walls of the minute arteries, and a hyaline granular change in the corresponding capillaries.

3. This change occurs chiefly outside the muscular layer, but also in the *tunica intima* of some arterioles.

4. The degree in which the affected vessels are altered, and the extent to which the morbid change is diffused over the vascular system of the different organs, varies much in different cases.

5. The muscular layer of the affected vessels is often atrophied in a variable degree.

They sum up their general conclusions as follows:—

1st. There is a diseased state characterised by a hyaline-fibroid formation in arterioles and capillaries.

2nd. This morbid change is attended by atrophy of the adjacent tissues.

3rd. It is probable that this morbid change commonly begins in the kidneys, but there is evidence of it also beginning primarily in other organs.

4th. The contraction and atrophy of the kidney are but part and parcel of the general morbid changes.

5th. The kidneys may be but little, if at all, affected, whilst the morbid change is far advanced in the other organs.

6th. This morbid change in the arterioles and capillaries is the primary and essential condition of the morbid state called chronic Bright's disease with contracted kidney.

7th. The clinical history varies according to the organs chiefly and primarily affected.

8th. In the present state of our knowledge we cannot refer the vascular changes to an antecedent change in the blood due to defective renal secretion.

9th. The kidneys may undergo extreme degenerative changes without being attended by the cardio-vascular and other lesions characteristic of the condition known as chronic Bright's disease.

10th. The morbid state under discussion is allied to the conditions of old age, and its area may be said hypothetically to correspond to the *area vasculosa.*

11th. The changes, though allied with senile degenertions, are probably due to causes not yet ascertained.

Such are the conclusions of Sir William Gull and Dr. Sutton, and they certainly appear to me to do little

towards the elucidation of the nature of the disease under consideration; and you will observe they do not fulfil the conditions I have already laid down as essential to the scientific discussion of morbid process—viz., that it should bear a relation to the departure from healthy action.

Putting out of consideration the lardaceous degeneration of the renal arterioles, Dr. Johnson maintains that the condition to which Sir William Gull and Dr. Sutton have applied the term "arterio-capillary-fibrosis" is of artificial production, and due to the effect produced on the normal *tunica adventitia* of the arterioles by immersion in glycerine and dilute acetic acid. "A sight of the preparations" (of Drs. Gull and Sutton), says Dr. Johnson, "convinced me at once that my surmise had been correct, and the so-called 'hyaline-fibroid' is neither more nor less than the normal *tunica adventitia*, probably hypertrophied together with the muscular coat, and certainly distended and rendered transparent by the endosmosis of the highly refracting glycerine fluid. The regular arrangement of the elongated nuclei with their long diameter in the direction of the arterial canal, and the entire absence of any abnormal appearance, afford conclusive evidence that the *tunica adventitia* has undergone no pathological change."* My own examination of this portion of our subject compels me to affirm my unqualified adherence to the views of Dr. Johnson.

These views are substantially confirmed by the recent observations of Dr. Grainger Stewart. † An examination of twenty-three cadavers afforded him the

* If the quantity of acetic acid be considerable the vessels become speedily decolorised, and the "hyaline-fibrosis" appears in a few hours.

† *Brit. Med. Jour.*, Nov. 15th, 1873.

following conclusions. Dr. Stewart observed, besides fatty granules in vessels, aneurisms of their walls, thrombi within them, and *a more or less marked thickening of the outer coat of the small arteries.* This, he says, is in some cases so distinct as to attract attention by its wavy, fibrous appearance, and the sinuous outline of the vessel, where no reagent has been applied. But these appearances become much more distinct when the specimens are placed for a short time in water or in glycerine, or when a little dilute acetic acid is added. "*The condition thus described corresponds exactly to the appearances of the specimens of so-called hyaline fibroid disease which I examined.*"

"*I found in several instances distinct thickening of the middle coat, with increase of the muscular fibres. I found no evidence of atrophy of this coat. Thirdly, I found the internal coat in some parts thickened.*"

Dr. Stewart has found the three coats thickened in the same artery, and he failed to find in the capillaries any evidence either of thickening or of exudation of their walls.

Of Dr. Stewart's 23 cases, in 12 the blood-vessels were healthy, 2 had the middle coat thickened, 3 to a marked extent, and 2 to a slight. There were 10 in which the outer coat was thickened, and 4 in which the middle coat was also thickened. Of the 12 in which the walls were natural there were—(1) Case of chronic peritonitis; (2) one of phthisis, with slight cirrhosis of the kidneys; (3) one of cystic disease of the kidney, fatal by uræmia; (4) one of slight cirrhosis of the liver and kidneys; (5) one of tubercle of the lungs, pleura, and peritoneum; and cerebral embolism: (6) one of typhoid fever; (7) one of pleurisy and

double pneumonia, and cerebral embolism; (8) one of cirrhosis of the kidney with aneurism; (9) one of phthisis, with combined waxy and inflammatory Bright's disease; (10) one of phthisis, with inflammatory and slight waxy disease; (11) one of induration, with slight cirrhosis of the kidney, and hypertrophy of the heart; ; and (12) one of waxy Bright's disease.

Of the 5 cases in which the middle coat was hypertrophied—(1) one was a case of inflammatory Bright in the second, passing into the third stage; (2) one was another example of the same disease, fatal by hæmorrhagic apoplexy; (3) one was a case of cirrhosis of the kidney, in which the kidneys were about the normal size—in these it was well marked; (4) one of perinephritic abscess with atrophy of one kidney, and compensating hypertrophy of the other; (5) one of advanced cirrhosis of kidneys and liver.

Of the 10 cases in which the outer coat was thickened—(1) one was a case of valvular disease of the heart, with congestion of viscera; (2) one was a case of inflammatory Bright's disease, fatal in commencement of third stage—the middle coat was also thickened; (3) one was a case of acute alcoholism; (4) one was a case of carcinoma of the uterus with hydronephrosis; (5) one was a case of typhoid fever; (6) one was a case of cirrhosis of the kidney—the middle coat also was hypertrophied; (7) one was a case of perinephritic abscess—the middle coat was here also somewhat hypertrophied; (8) one was a case of inflammatory softening of the cord; (9) one was a case of commencing cirrhosis of kidneys and liver; and (10) one was a case of advanced cirrhosis of kidneys.

In 12 cases of Bright's disease the vessels were

natural in 7. Of these 7, one was a case of waxy degeneration, 2 of waxy and inflammatory disease combined, and 4 of cirrhosis. Morbid conditions of vessels existed in the remaining five cases, of which three were cases of cirrhosis, and two of inflammatory disease. One of the last-named had the outer coat natural.

These facts seem to indicate, continues Dr. Stewart —1st, That the waxy forms of Bright's disease, and the inflammation in its early stages, have no relationship to the state of the vessels under consideration [this I have already endeavoured to explain]; 2nd, That in regard to cirrhosis, although changes in the vascular walls were present in 3 cases, they were absent in 4. There seems, therefore, Dr. Stewart thinks, to be no constant relationship between the one condition and the other. Of the 10 cases in which the outer coat was thickened, there were 6 in which there was no Bright's disease whatever; but the middle coat of the arteries was hypertrophied in 5 cases, and 4 of them were cases of long-standing Bright's disease, while in the fifth one kidney was destroyed. This condition occurred in *none of the whole series that was not renal.* With respect to the relationship between the state of the vessels and hypertrophy of the heart, Dr. Stewart's cases furnish the following evidence:—In 12 of the cases noted as normal, the heart was hypertrophied in 4. Of the 5 cases in which the vessels had thickened middle coats, the heart was hypertrophied in 4, and all of them were cases of Bright's disease. Of the 10 cases in which the outer coat was thickened, it was hypertrophied in 5, of which 4 were cases of Bright's disease, and 1 had valvular affection, while it was normal in 3 and small in 2. It should be stated that Dr. Stewart's experience differs from that of

Dr. Johnson as to changes in the renal epithelium. He says, "I have not in these cases found changes in the epithelium, but have never failed to find increase of the connective tissue."*

Analogous Changes in other Organs.—The organs most frequently affected coetaneously with the kidneys in Bright's disease, and presenting similar pathological conditions, are the liver, the spleen, and the pancreas. In a secondary manner the intestines and the peritoneum are occasionally affected; leaving out of consideration at present the organs liable to œdema, and the diseases of the vascular system, and the cerebral disorders arising from associated apoplexy and blood-poisoning.

With respect to the *liver*, Dr. Bright found it sound in 40 cases out of 100, the change was slight in 35, and serious in 18 cases. Rayer's experience gives affection of the liver in a third of his cases, in some throughout its entire extent, in others only partially. It was enlarged in a small portion of cases—a sixth—and chiefly in those cases where there coexisted cardiac affection. Occasionally a portion of its peritoneal surface was adherent to the adjacent parts. In a few cases it was softer than natural, but more frequently harder, indurated, and diminished in bulk. In the latter case its surface was irregular, and of a deeper colour than usual. On section diverse morbid colours are presented. Sometimes it is pale and anæmic, its vessels containing very little blood. At other times, on the contrary, the liver presents a deep congested colour. The two conditions may co-exist in the same liver. In other cases irregular yellowish patches are apparent on the surface of the

* *Vide* Dr. Grainger Stewart's Paper, *Brit. Med. Journal*, Nov. 15th, 1873.

liver, interspersed with an irregular colouration of a deeper red colour than the healthy organ. These pale and red colourations occasionally prolong themselves into the interior of the organ. As in affections of the kidney the liver sometimes offers a kind of exaggeration of the natural aspect of the organ. On section it appears as if granulated. This appearance seems due to a congestion of the vascular substance of the organ, by comparison with which the other portions seem paler.

As in the case of the kidney, the tissue of the liver may become the seat of fatty degeneration. The hepatic cells become loaded with fat, and the etiology is doubtless the same as in the corresponding renal affection. This condition is frequently coexistent with an increase of the interlobular connecting tissue of the hepatic parenchyma, which is an essential feature of cirrhotic degeneration; and hence Gluge and Leréboullet were led to the conclusion that cirrhosis proceeded from deposit of fat in the hepatic cells. Gluge called this particular form of cirrhosis "steatose;" and described another which he believed to be due to interlobular hepatitis. In chronic cachectic nephritis fatty granulations of the liver are not unfrequent, and it cannot be doubted that they have a close affinity with the same appearances in the kidney—nay, that they are manifestations of the same constitutional diathesis. When the liver presents these granulations it is generally harder than in its normal condition.

In the true cirrhosis of the liver—the hob-nail liver of drunkards—and the analogue of the corresponding affection in the kidney, the external surface of the liver is darker in colour, crimpled and irregular, and considerably diminished in size. When divided, the natural

appearance is in a great measure removed, and the section presents a tuberculated surface, infiltrated with a yellowish material, grating under the scalpel; the calibre of the vessels is diminished. Furthermore, chronic atrophy of the liver presents another correspondence with the like condition in the kidney, in that the walls of the portal vein are remarkably thickened, and that in the advanced stages there is total destruction of the hepatic capillaries, and shrivelling or complete disappearance of the secreting cells. This affection of the liver causes death by the retention of bile products, just as that of the kidney does the same by retention of urinary products.

The waxy or lardaceous degeneration of the liver in like manner presents analogies to the corresponding condition of the kidney. The initial change takes place in the gland cells; the appearances are ill-defined, and easily overlooked. The first indication is that the middle portions of the lobules become reddish-yellow, translucent, and firmer than natural, and sharply defined from the surrounding dull grey rim, and hence the lobular structure is usually distinct. A solution of iodine developes glistening pellucid places everywhere, of a deep red colour, the surrounding rim being only pale yellow. Ultimately the minute vessels of the liver become affected in a similar way, just as those of the kidney, their walls becoming thickened, homogeneous, and lustrous, and their channel narrowed, sometimes entirely obliterated.

In treating of the structural changes which the renal tissue undergoes in cases of nephritis, I alluded to what may be regarded as a pathological law, that *depraved blood determines the formation of lower forms of tissue*,

relatively to the departures which it presents from its normal constitution. This position was supported and illustrated by reference to certain morbid changes. Amyloid degeneration, wherever it occurs, stands in this relation to altered blood. The precise mode of formation, according to Dr. Dickinson, is that the amyloid substance is nothing else than fibrine deprived of the free alkali which normally enters into its composition. In support of this view he adduces the following facts:—1st, That compared with albuminoid substances amyloid matter is simply characterised by the absence of free alkali; hence, in the amyloid liver a fourth less at least of alkali (potash or soda) exists, compared with what obtains in the case of the normal liver. 2nd, The amyloid liver loses the property of being coloured by iodine, if it be macerated primarily in an alkaline solution. I confess that I attach little importance to the pathological bearings of this fact, when it is considered that the presence of an alkali, *independently of that of the amyloid or other structure, destroys the colour of iodine.* Finally, Dr. Dickinson supports his view by the artificial preparation of a substance resembling that known as amyloid. By dissolving fibrine in dilute hydrochloric acid (1. 10,000); then evaporating, the fibrine is thus deprived of its alkali, and presents the appearance of a gelatinous substance giving reactions similar to those of amyloid matter.

Etiological conditions support this view, in the fact that the amyloid changes of internal organs coincide so frequently with prolonged suppuration (caries, phthisis, ulcers, &c.), and that pus is a liquid rich in albumen and alkaline salts; the blood thus becomes

relatively rich in fibrine, and poor in alkalies. Altogether, this theory may be regarded still *sub judice*.

As to the influence of alcohol in the productions of affections of the liver, there can scarcely be said to be a difference of opinion among physicians, and Budd consequently remarks that spirits are more injurious when taken undiluted and on an empty stomach. Different views have been entertained as to the intimate nature of fatty liver: Andral, Thomson, Barlow, and Cruveilhier, &c., regard it as a form of atrophy. I do not regard it primarily as atrophy: the atrophy is secondary, and consequent on the degeneration of the secreting cells, as in the case of the kidney; and the opinion of Leréboullet singularly coincides with what I have advanced regarding the purposes to which fibrine is applied in the liver (*vide* pages 67 and 75), and my view of fatty degeneration in the kidney. This authority remarks:—"Le développement de la graisse dans ces cellules parait étroitment lié *a un ralentissement* dans le travail nutritif, et *a la combustion* organique, qui est la première condition de ce travail." I say, this sentence accords in a remarkable manner with the phenomena of fatty degeneration, diminished temperature in uræmia, and the views of pathology advanced above.

Affections of the Spleen and Pancreas in Cachectic Nephritis.—In almost all instances in which the liver is affected as described, the spleen presents corresponding structural changes. Dr. Grainger Stewart has found its capsule thickened and its structure fibrous in 33·3 per cent. of cases of Bright's disease. The spleen is sometimes considerably enlarged: Rayer has seen it four times the normal volume, and full of fatty granulations similar to those which occur in the liver. In other

cases where there are no granulations, the organ is friable, sometimes soft, sometimes hard and firm. In general it presents a deep colour; but on section its tissues sometimes present an appearance similar to a slice of mottled sausage; at other times it is pale, exsanguine, and flabby, its texture extremely transparent, and the finger with difficulty penetrating in its structure. The spleen is sometimes the seat of tubercular matter, but this in connection with Bright's disease is a mere coincidence. Rayer has seen the spleen the seat of a large sack which communicated with the stomach.

The *Pancreas* is very seldom diseased in cases of chronic nephritis. Bright found it congested in one case, hard and firm in some, and obstructed in one case. In phthisical cases tubercular deposits have been found in it. Rayer never saw it different from the healthy condition in nephritis. Disease of this organ has appeared in some cases in the course of pregnancy. Taking the various pathological appearances together, the etiological conditions, the anatomical and physiological similarities of the kidneys, the liver, and spleen, it cannot be doubted that their affections, in conjunction with cachectic nephritis, are not mere coincidences, but proceed from the same constitutional diathesis.

Among the diseases with which cachectic nephritis is not unfrequently coincident may be enumerated bronchitis, pneumonia, pleurisy, phthisis, psoriasis, scarlatina, syphilis, &c. The discussion of these, however, would simply be the discussion of the diseases themselves, would throw no light on the subject of cachectic nephritis, and are beyond the limits assigned to these remarks.

LECTURE V.

Theory of Uræmic Poisoning—Vicarious Elimination; by the skin, bowels, &c—Injection of Urea into the Blood; its effects—Dr. Owen Rees' theory of Uræmic Poisoning—Traube's theory—Experiments of Traube, Kussmal, and Tanner—Bence Jones on Uræmia—Frerichs, Freitz, and Jaksch, Sherer, Hoppe, and Oppler, on Uræmia—Cerebro-spinal Symptoms in Uræmia—Varieties of Nervous Complications; the Convulsive form; the Comotose form; the Mixed form; and Rare form—Diagnosis of Cachectic Nephritis—Tests for Albumen in the Urine.

GENTLEMEN,—Until very recently the opinion was generally entertained that one of the most formidable complications and most ominous of approaching death —viz., the epileptiform convulsions and the succeeding coma, which frequently terminate the protracted illness in cases of cachectic nephritis,—were due to the retention in the blood of urea; hence the terms uræmia and uræmic poisoning—terms which ought to be discarded if a nomenclature conformable to pathological conditions is desiderated. The idea, then, that the convulsions met with in chronic Bright's disease are due to urea is one, as I shall show you, not longer tenable.

Theory of Uræmic Poisoning.—In cases of epilepsy it may be received as a universally admitted fact, that the immediate cause of the convulsions is a sudden deprivation of blood from the brain or particular portions of it; and I should infer, in addition, congestion in other

portions, and that it is not impossible that this condition may be the immediate cause of the phenomena in question. It is well known to what an extent reflex irritation operates as a factor in the production of this state. It may therefore be said that convulsions are produced in a twofold manner, the one physical—an interruption to the current of blood, as from embolism, &c.,—the other physiological, *i.e.*, through causes operating on the nervous centres, and in turn on the minute arterioles, probably contracting them and disturbing the normal balance of the circulation. But again, poisoned blood may lead to structural changes in the brain as elsewhere; hence the albuminuric retinitis, so-called, disease of the vessels of the brain, and the possible contingency of cerebral hæmorrhage. All this does not militate, however, against the belief that the convulsions may be due to one or other of the retained urinary products; but that this product is urea, the facts proving the contrary are so numerous and so overwhelming that the idea cannot be rationally entertained.

While it is perfectly true that there is no such thing as complete vicarious elimination, it is equally true that between the skin and the kidneys there is a functional co-ordination neither unimportant nor very limited. Hence, in cases of anuria, urea is eliminated by the skin as well as doubtless by other excretory organs. Desault therefore remarks: "Il est vrai que la nature prévient quelquefois les accidens ou retarde leur naissance en se débarrassant en partie des urines, par d'autres emonctories, tel que la peau, les oreilles, les narines, la bouche, les mamelles, l'anus, &c." Dr. Johnson* mentions a

* London Medical Commentaries, vol. v.

case of suppression in which for some days before death the skin was all over as white as if it had been powdered: this white dust, when gathered, was found to have the taste of crude sal-ammoniac. This ammoniacal salt, presuming it to have been such, might have resulted from the decomposition of urea. According to Schottin, in cases of a similar nature urea is found in pus, and milk, and the sweat may contain so much of it as to form a dust on the skin. More recently, Dr. Deininger* published the case of a boy, æt. 5, who suffered from anurea renalis for a whole week, and on whose skin urea was discovered. Five cases of this kind have been recorded by Jürgensen and Leube, but the issue was fatal in their cases, whereas Dr. Deininger's patient recovered. In none of these cases are we informed that there were convulsions. But not only does the skin sympathise vicariously with the kidney, but there is every reason to suppose from analogy and post-mortem appearances that the diarrhœa which is so frequent and so capricious in Bright's disease—a symptom, by the way, noted by writers of the greatest antiquity,—can be regarded in no other light than that of a vicarious flux. This diarrhœa comes on suddenly, disappears suddenly, and is little under the influence of medicinal agents; it is frequently serous, and abundant, as in cholera, and weakens the patient to such an extent that he often regards it as the major ailment.

However abundant that diarrhœa may be it does not diminish the dropsy; indeed, it is not rare to find an augmentation of both conditions concomitantly.

Post-mortem examination reveals the intestinal tract

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* Deut. Arch. Klin. für. Med.

either healthy in appearance or discoloured; or rather it offers such slight textural alterations as not to explain its derangement during life. Bright reports a case of this description, where the duodenum was found very vascular. Hodgkin has seen the ilium very much injected and of a purple colour, but without ulceration or any alteration in the intestinal follicles. Rayer has observed the small intestine affected in the same manner either solely in that state or conjoined with other pathological changes. Christison relates a case where the mucous membrane at the termination of the ilium and the commencement of the colon was of a chocolate colour and soft. Martin-Solon has seen the mucous membrane of the last convolutions of the ilium, the end of the colon, and all the rectum, thickened, greyish, interspersed with reddish patches, small points, and vascular arborisation. In a case of Gregory's there were red patches and ecchymoses in the small intestines; in short, the appearances which the intestinal tract presents have a close analogy to the condition of the kidney, and the other organs mentioned, as being occasionally implicated in the general morbid process. That this condition represents the elimination of material incompatible with the healthy functional action of the bowels there can be no reasonable doubt.

While from this point of view, urea does not appear to be the immediate cause of convulsions, direct experiments prove that its introduction into the blood is not followed by convulsions; or if symptoms of poisoning occur, that there is a marked disparity between the quantity necessary to produce these phenomena and that which is found in the blood in cases of so-called uræmic poisoning. Thus, Gallois has demonstrated that in the

rabbit 28 grammes of urea must be introduced into the stomach to produce toxic effects. Bright, Christison, Schottin, and others have proved in like manner that urea can exist in considerable quantity in the blood without causing death; and Parkes, Schottin, and Mossler have shown that urea may be increased in the urine, even beyond its normal quantity, in uræmia. Hammond, it is true, has obtained results somewhat different, and insisting that the healthy kidney permitted the elimination of the urea injected, submitted the animal to nephrotomy. But this is assuredly a serious mutilation, and one which complicates the experiment to such an extent as to nullify the results; the shock of the operation might alone suffice to cause death.

Having regard to the altered condition of the blood in uræmic subjects, Dr. Owen Rees desired in this to find an explanation of the nervous symptoms, believing them to be due to local effusions on certain portions of the cerebral substance. A similar theory was propounded by Traube. According to the latter, two factors were to be considered—

1st, A diminution of the density of blood serum *(Verdunnung Blutserums)*.

2nd, Augmented tension of the vascular system.

"If by any cause whatever that tension becomes heightened, or if the serum of the blood suddenly becomes less dense, cerebral œdema is produced, which in turn occasions coma and convulsions. The nature of the uræmic symptoms depends on the extent to which the encephalon is involved in the morbid process."

Münke,* in a communication to the Society of

* Ueber Uraëmie, von Phillip Münke. Berl. Klin. Woch. 1864.

Medicine of Berlin, having explained his reasons for rejecting all other theories, affirmed his adherence to that of Traube, contending that it accorded with facts. To prove this, he had recourse to the following experiment:—Having ligatured the two ureters and the right jugular vein in a dog, he injected water into the left carotid artery. The animal gamboled, and fell into a comatose condition, during which violent convulsions took place, and death resulted in eighteen hours after the injection. Münke observed the same results in all similar experiments. Blood defibrinated and injected similarly produced like results. Microscopic examination revealed an anæmic and œdematous condition of the brain, and the convolutions were more or less effaced. He never witnessed effusions of blood on the brain in consequence of the injection of water. His conclusion is in the following terms:—"We have proved, then, that when in addition to a diminished density of the blood there exists an exaggerated arterial tension persisting during some time, the symptoms commonly called uræmic do not fail to be produced."

Münke has further desired to discover whether the diminution of the blood tension after ligature of the ureters would have succeeded in warding off uræmic complications; and he accordingly tied the two carotids in dogs, having previously tied the ureters, when it was found, that while nausea and vomiting were produced, neither coma nor convulsions ensued.

Contrary to the experience of Traube, Kussmal and Tanner have produced results diametrically at variance. In interrupting the circulation of blood towards the head, either by ligature or pressure of the carotids, epileptic convulsions were thus caused, which vanished

when the obstacle was removed, and the free circulation of the blood restored.

Bence Jones ascribed the phenomena of uræmic convulsions (and the term may be provisionally retained for convenience' sake) to oxalic acid, but the presence of this acid in the blood is doubtful; and when introduced into it gives rise to different symptoms.

From these considerations, Frerichs, in 1851, expressed the opinion that in the presence of carbonate of

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The following woodcuts refer to the text in pp. 89-90 *antea*:—

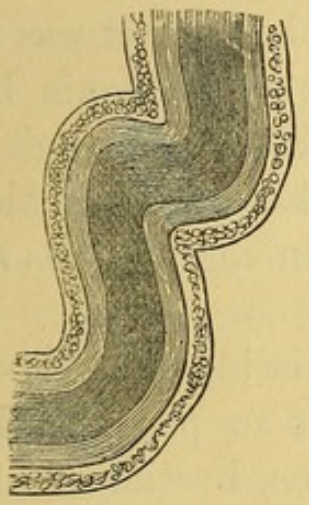

FIG. 18.

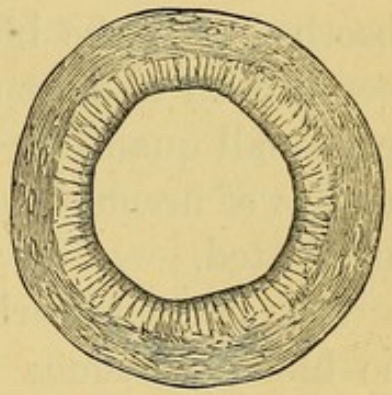

FIG. 19.

FIG. 20.

FIG. 18.—Artery from the kidney, with hypertrophied muscular walls, showing internal and external muscular fibres of about equal thickness. Canal injected × 200.

FIG. 19.—Transverse section of hypertrophied renal artery × 200.

FIG. 20.—Normal renal artery × 200.

ammonia in the blood was found the solution of the difficulty. According to this authority urea encounters in the blood a special ferment which converts it into carbonate of ammonia. The existence of this ferment has never been demonstrated; and the only proofs supporting this view, even according to Frerichs, are a violet colouration of the blood, the presence of carbonate of ammonia in the vomited matters, and the dejections. These proofs are certainly of doubtful value, and hence the theory at issue must be held as unproven.

In 1860 this theory was modified by Treitz and Jaksch, who maintained that the conversion of urea into carbonate of ammonia took place not in the blood, but in the intestines, and that in this form it was re-absorbed into the blood. Carbonate of ammonia has been proved to exist normally in the blood, although in very small quantity; and Rosenstein has remarked that in cases of uræmia the quantity therein contained is *not* augmented.

It is true that carbonate of ammonia introduced into the blood occasions convulsions; but to produce this effect the quantity must be large; thus, Frerichs found that it was essential to the production of these phenomena to introduce into the blood of the dog no less than from one to two grammes. Injected into the frog, clonic convulsions are produced, but not the other phenomena of uræmic poisoning, especially the epileptiform convulsions and the coma; and relatively to the weight of the animals operated on, Rosenstein has remarked that to produce the same consequences in man from 20 to 30 grammes of carbonate of ammonia would be requisite, a quantity which would be easily demonstrated in the blood by chemical appliances; yet the merest traces of

this agent are found in the blood of persons who die from so-called uræmic poisoning.

It is worthy of further remark that Jaksch* pointed out in 1860 a distinction between the symptoms which supervene on arrested secretion of urine—or *uræmia* properly so-called—and those that follow resorption of urine which had become ammoniacal. To the latter he applied the term *ammoniæmia*. In such cases it was pointed out that the breath and urine give off an ammoniacal odour, that rigors are frequent, that vomiting is invariable; while in the former case—in uræmia of Bright's disease—neither the breath nor urine exhales this odour, there are no rigors, and vomiting may be wanting.

Again, dropsy is not observed in cases of *ammoniæmia*. Rigors are, however, a frequent accompaniment, and of such a nature as to simulate intermittent fever. The tonic and clonic convulsions which distinguish uræmia are wanting in ammoniæmia; and in the latter albumen is sometimes found in the urine, but always in conjunction with mucous or pus. Further, in ammoniæmia the derangements of vision are absent, in common with the characteristic appearances of the eye, which mark a true case of Bright's disease. There is an absence of the vomiting, diarrhœa, and pulmonary complications so common in genuine nephritis. Constipation rather than diarrhœa is complained of, the tongue is dry—the opposite condition being characteristic of nephritis,—jagged, and covered with a blackish coat. The mucous membranes of the mouth, larynx, nose, and eyes are dry; the skin becomes dry; the tissues of the body

* Prager Vierteljahrschrift. 1860.

waste, the respiration is normal, but the intelligence, contrary to what obtains in uræmia, remains unclouded till the last.

In 1868 M. Sée affirmed his adherence to this differentiation. Jaksch goes yet further, in distinguishing two forms of ammoniæmia: under the first division he embraces all the cases wherein the accumulation of carbonate of ammonia in the blood is due to resorption of the salt produced by the transformation of the urea in the digestive canal; under the second, such as are occasioned by the resorption of stagnant and decomposed urine.

Scherer, Hoppe, and Oppler, recognising the insufficiency of the foregoing views to explain the phenomena of uræmia, have attributed the uræmic symptoms to the retention of inferior products of oxidation, such as creatin, creatinine, leucine, and kindred other *extractive matters*. Oppler has found these substances augmented in the fluids of the body, and even in the muscles. Chalvet recognised in the presence of these matters an indication of diminished organic combustion—a view which again accords with that which I have advanced regarding the pathology of fatty degeneration of the kidney and liver, and the production of urea in the latter organ. While it is not possible, then, in the present state of our knowledge, to condescend with certainty on the particular agent which gives rise to the nervous complication in cachectic nephritis, we seek in vain for pathological changes in the cerebro-spinal system as invariable concomitants of this condition. It is true that in certain cases sub-archnoid serous effusion is discovered; or, in other cases, the ventricles and base of the brain are the seat of consider-

able effusion. Barlow,* by treating this fluid with nitric acid, has obtained nitrate of urea.

Sometimes, though more rarely, there exist symptoms of genuine arachnitis—the arachnoid is thickened, or opaque; but it is noteworthy that *this condition has been found in cases where, antecedent to death, the coma and convulsions were absent.* Bright, Christison, and Gregory have observed cerebro-spinal symptoms in cases in which post-mortem examination revealed an ex-sanguine condition, and others in which the substance of the brain was vascular or red. In 400 cases, Frerichs and Rosenstein† found arachnitis in only nine. That the convulsions are due to inflammatory complications is therefore an hypothesis that must be rejected.

The view adopted by Traube, and the one I believe now most generally followed, is, that whatever be the disturbing agent, it acts by causing an impression on the vaso-motor nerves, whereby contraction of the cerebral arterioles follows, and consequent anæmia of the brain. It must not be concealed, however, that while this view may satisfactorily account for the coma, it fails to do so for the convulsions and delirium.

Taking all the circumstances into consideration, there is nothing which accounts for the uræmic manifestations so satisfactorily as that which regards them as due to the presence in the blood of various extractive,

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* Bright, "Guy's Hospital Reports," No. 11, 1836, p. 353.

† Quite recently *(Lyon Med.)* Rosenstein has noticed the coincidence of albuminuria with meningitis. In nearly all the patients of this class albumen was found in the urine in the early stages of this affection. In a considerable number of them tube-casts, blood-globules, and epithelium cells were found, just as in genuine cases of Bright's disease. The lesions found after death were similar to those of cachectic nephritis. The kidney was increased in size, the hypertrophy being chiefly confined to the cortical portion; the renal tissue was injected, and the glomeruli injected with blood, with extravasation of blood into the urinary tubules.

imperfectly oxidised matters. This theory *not only accords with all the views already advanced, explains all the phenomena*, but is in harmony with direct experiment. Schottin,* as early as 1853, renounced all other theories in preference to this one. In the following year Reuling corroborated Schottin's views; and Hoppe† having had occasion to examine the body of a patient who died of uræmic symptoms consequent on cholera, found in the muscular tissue a large quantity of creatine. An analysis of the blood gave in 1000 parts—

	1.27 of Urea.
	8.60 of other Extractive Matters.
Total of Extractive Matters,	9.87

An enormous disproportion, relatively to extractives, is thus apparent between the composition of healthy blood and that which exists in uræmia. The muscular tissue of the same patient gave 159 grammes per pound. These conditions, it is worthy of note, are in perfect accord with the pathological manifestations of cholera, and the curative means adopted, and most successful in combating the disease.

Oppler has never succeeded in finding carbonate of ammonia in the blood of animals submitted to vivisection; but, on the other hand, he has found an excess of extractive matters in the proportion of from 18 to 19 per 1000. The muscles contained a large quantity of leucine and creatine—as much as 2.2 grammes of creatine per pound. The researches of Perls‡ and Zalesky in like manner confirm this view. Perls found in the muscular tissue of uræmic subjects a large excess of

* Beiträge sur Charasteristik der Urämie in Vierord's Arch.

† Dritter Arztlicher Bericht über das Arbeitshaus im Jahre. Berlin. 1854.

‡ Beiträge zur Lehre von der Uramie, t. x, p. 56

urea, of creatine, and other nitrogenous extractive matters. Zalesky found that these matters varied in the following proportion, under the subjoined conditions—

Muscular tissue of Healthy Animal,.....	grammes	%	0.060
,, ,, after ligature of ureter,	,.		0.280
,, ,, Nephrotomised Animal,	,,		0.531

All the facts tend to show that the normal transmutation of tissue by means of oxidation is arrested; and it is highly probable that the nervous structures undergo changes in like manner, which manifest themselves in the manner about to be noticed.

With regard to the urinary secretion, in relation to uræmic poisoning, Bright has seen the nervous complications succeed to cases of dropsy with coagulable urine, or in cases in which the urine contained albumen, but where dropsy was absent. I have myself seen both. Christison has noticed that the complications in question were not necessarily coincident with diminished secretion of urine. He has seen coma come on in a case where the patient voided thirty ounces of urine per diem; on the other hand, he has seen the urine reduced to a fourth of its normal quantity without the supervention of cerebral symptoms. According to Christison, the coma may occur early, or in the advanced stages of the affection in an equal degree. The early occurrence of coma is, however, more peculiar to cases of scarlatina, and I can bear my testimony to the opinion that the gravest cerebro-spinal complications may be recovered from in these cases, while in cachectic nephritis they are almost necessarily fatal.

Varieties of Nervous Complications.—Antecedent to the occurrence of the nervous complications, however, as *a rule*, the quantity of urine secreted is diminished; usually it contains less urea, the quantity is reduced

from 20 to 32 grammes for twenty-four hours, to 20, 10, or even 7. The chlorides are diminished in the same proportion, being reduced, as in inflammatory affections, from 11 grammes to 1 or 2 grammes; the same obtains with respect to the phosphates. On the other hand, according to Schottin and Chalvet, a marked increase of extractive matters exists in the urine: and, according to Frerichs, the quantity of albumen may be estimated at from 5 to 25 grammes. Though the *quantity* of urine may be about normal, its density is diminished; from 1025, which may be regarded as normal, it falls to 1015 to 1008. The acid reaction of the urine is generally feeble, except at the commencement of the disease. In the acute form of the disease the complications under consideration come on suddenly, and without warning, in many cases. In others there is sharp headache, sometimes frontal, sometimes occipital. The latter has been regarded by some as the special precursor of the convulsive form of uræmia. At the same time, there is insomnia and nocturnal agitation, symptoms which contrast strongly with the usual apathetic condition of the patient; memory is impaired, bodily movements are slowly performed, and hearing is obtuse.

Sometimes the first symptom is sudden loss of sight—a symptom which must not be confounded with a parallel condition associated with albuminuric retinitis in chronic Bright's disease.* Not unfrequently persistent vomiting ushers in this stage of it—a symptom which no condition of the stomach exists to explain.

* M. Crocq (note, sur l'amaurose comme symptôme de l'urémie—*Presse. Med. Bel.*) regards the amaurosis of uræmia as due to subretinal œdema; and Favel, in like manner, regards the aphonia of albuminuria as a symptom of œdema of the vocal cords.

At other times an habitual diarrhœa and vomiting may be suddenly arrested, when the nervous symptoms supervene so suddenly as to justify the belief in the vicariousness of the intestinal and gastric derangement.

The sphincters of the bladder and rectum become paralysed before marked symptoms of cerebral effusion appear, as I have quite recently seen. On other occasions local convulsions alone constitute the earliest symptoms.

However the nervous symptoms may be foreshadowed, they present in their totality such marked distinctive features as to justify their division into three forms:—1. *The Convulsive Form;* 2. *The Comatose Form;* 3. *The Mixed Form;* and M. Fournier adds a 4th, *The Rare Form (formes rares).*

Convulsive Form.—This form presents the following characteristics:—It is subdivisible into three *varieties*—the first, the *eclamptic*, is ushered in by sudden loss of consciousness, with tonic convulsions at the outset; then the clonic form, followed by somnolency, coma, and stertorous breathing—the condition resembles very much a true epileptic seizure. There exist, however, the following differences: the absence of the premonitory cry of epilepsy; and here there is frequently a pallor of countenance. Especially in this condition is there a distinctive absence of the unilateral preponderance of convulsions so characteristic of true epilepsy; again, in these cases the thumb is not contracted in powerful pronation on the palm of the hand. In epilepsy, reflex sensibility of the mucous membranes remains; in the uræmic eclampsia it is absent. Frothing at the mouth and biting of the tongue are *not usually*

observed in uræmic convulsions, though rarely these symptoms are noticed. Usually, the clonic convulsions are general; but sometimes *localised convulsions* do occur, so as to constitute another variety.

In other cases true *tetanic* attacks occur, with opisthotonos and trismus. These cases are rare.

The convulsive form, then, comprises three varieties —the eclamptic, the local convulsive, and the tetanic.

The Comatose Form.—This form may either be the termination of the convulsive form, or may be of sudden accession, *sui generis.* It is *incomplete* or *complete.* It is in the latter case that it is sudden, and of grave import. The face is pale; there is absolute insensibility. The pupils are sometimes normal, or sometimes dilated and sluggish under the influence of light. The patient is in a deep coma; there is stertorous breathing; and Addison has endeavoured to show that the stertor is differently produced from that existing in true epilepsy and cerebral apoplexy. In the latter he maintains that the stertor is caused in the nose and throat, while in the former it is caused alone by protrusion of the lips.

There is yet another distinctive character. The muscular relaxation and insensibility are general in uræmia, and not confined to one side, as they usually are in apoplexy and epilepsy. Furthermore, the uræmic coma is very insidious in its progress.

The Mixed Form, as its name implies, is a combination of the two preceding varieties; sometimes the *convulsive*, and sometimes the *comatose* form predominates.

Among the *Rare Types* are—1st, Those cases in which delirium constitutes a marked feature. Sometimes the delirium comes on as a complication in the convulsive form; but it may exist alone, and thus

specially constitute this variety. At other times it comes on abruptly, or may be preceded by the usual premonitions of uræmia, cephalalgia, impairment of vision, obtuseness of intelligence, slowness of movement, &c. 2ndly, The delirium may be monotonous, distinguished by incessant low muttering. Or, 3rdly, *Maniacal*, in which the patient is in continual dread of being pursued, and appeals for succour. A very rare form still is that in which *dyspnœa* is a notable characteristic. This form, of course, must be distinguished from œdema of the glottis, a complication, as we have seen, not unfrequent in Bright's disease. The latter—that arising from œdema of the glottis—is usually of slow progress, and its intensity varies according to that of the localised œdema in other parts of the body.

The other form—the true dyspnœic variety of uræmia—comes on suddenly; it rapidly glides into the terminal coma, and causes death often in three or four hours. This condition is further characterised by a marked absence of physical signs of lung disorder corresponding to the difficulty of breathing. Christison has seen tracheotomy practised twice in cases of this kind, no trace of œdema of the glottis being disclosed.

On analysing the symptoms comprising uræmic convulsions, it is a fair and legitimate deduction that the variations presented depend on the particular portions of the cerebro-spinal axis affected. Thus, the eclampsia points to an excitation of the medulla oblongata; the tetaniform convulsions to a like impression on the cervical portion of the spinal marrow; the partial convulsions indicate an impression limited to particular nerves; the intellectual aberration indicates irritation, particularly of the surface of the hemispheres; and in

the form where dyspnœa predominates, it cannot be doubted that the part of the nervous system affected is the origin of the pneumogastric nerves, in the fourth ventricle; while, in the cases where the dyspnœic symptoms are complicated with sibilant respiration, it is probably the laryngeal nerves that are paralysed, as aneurism of the aorta produces the same phenomena by pressure on the recurrent laryngeal.

Diagnosis.—The diagnosis of acute nephritis offers much less difficulty than that of the chronic form. The sudden occurrence of dropsical effusion into the peritoneum, the pleura, the pericardium, &c., with albuminous urine of high specific gravity, frequently containing blood, and febrile disturbance, are sufficiently characteristic. In the absence of albuminous or bloody urine —a circumstance rare in acute nephritis—the indications may be more equivocal.

The affection with which nephritis is most likely to be confounded is hæmaturia. It is to be distinguished from the latter by the following circumstances:—In hæmaturia fibrinous concretions, or even clots of blood, are usually found in the urine, and usually the renal region of one side is more tender on pressure than the other; the urine is generally voided with pain, and there is an absence of dropsy. Hæmaturia from contusion and renal calculi is not likely to be confounded with the bloody urine of nephritis.

In many acute diseases the urine may contain blood; but the history of the case, and the presence of clots and urates, clear up any uncertainty. In exceedingly rare cases, supervening on scarlatina, anasarca may occur without notable changes in the urine.

The *diagnosis of chronic nephritis* is attended with

much more difficulty, and for the following reasons:—Dropsy may be produced by other causes; the urine may contain albumen in conjunction with affections of the heart, liver, lungs—in short, owing to any condition which interferes with the free circulation of blood through the kidney. But when little or no pain is complained of in the lumbar region, when urine of a *light specific* gravity is passed, containing no urates and a considerable amount of albumen, and no disease of any other organ exists which might account for the albuminuria, the diagnosis may be made with certainty. In the albuminuria from static congestion the specific gravity of the urine is almost always normal, the urea of the urine is not diminished, and the presence of albumen in the urine may be said to be capricious, depending as it does on the position of the body; thus, it may entirely disappear if the recumbent position be observed. Diabetes is sometimes complicated with the presence of albumen in the urine. It is well known that in the diabetic the condition of the blood and the elimination by the kidney of, to it, a morbid product, induces in it structural changes; but the presence of sugar in the urine is a sufficiently distinctive feature to prevent error.

The presence of pus in the urine, in such cases as pyelitis and cystitis, may be mistaken for albuminuria. When the urine contains pus it necessarily contains albumen, which is one of the ingredients of pus. The reaction of liquor potassæ and ammonia on urine containing pus, with the general symptoms, should be sufficient to prevent mistake on this point.

If, after a short interval, cerebral symptoms and vomiting, even without dropsy, take place; if the urine

be of a light specific gravity; if there be an absence of indications of disease in any other organ—the existence of chronic nephritis is more likely, than a cerebral affection, as a primary disorder. This would he confirmed by a history of exposure to cold, alcoholic indulgence, and the existence of general dropsy even at a somewhat distant date. If, in addition to all these symptoms, anasarca or effusion occur, the diagnosis is absolutely certain. The appearance of epithelial cells and casts does not *immediately* bear upon diagnosis, as we have seen that they occur coincidently with other diseases. But should hypertrophy of the heart, with valvular insufficiency, or disease of the liver, be present, the diagnosis is rendered yet more difficult. In such cases, moreover, the urine is sometimes of lighter specific gravity than it is in health, and it not unfrequently contains albumen. How are we to determine that the renal affection is primary, not secondary? Or may not the albuminuria be dependent on the simultaneous cooperation of the two causes? As a rule, dropsies dependent on affections of the heart usually begin in the inferior extremities, and disappear during the observance of the horizontal position; dropsies dependent on renal affections generally begin in the face, giving to it a characteristic puffiness which the experienced eye so certainly recognises as not usually to confound it with any other condition. It is rare that the dropsy is so general in cases of simple affection of the heart, as when complicated with cachectic nephritis. In the dropsy due to affection of the liver the urine is usually scanty, of a dark, *bilious* colour, ascites is specially characteristic, and albumen is absent from the urine. In cases in which affection of the liver and kidney are concomitant,

while it may be difficult to say to what extent either contributes to the production of dropsy, the affection of the kidney is recognised by the low specific gravity of the urine, and its contained albumen.

So much for the general diagnosis. A more minute analysis of the symptoms is capable of demonstrating with tolerable certainty the special form of Bright's disease. The parenchymatous nephritis is more especially a disease of early life, and occurs frequently from exposure to cold, damp, and scarlatina. It runs a rapid course compared with interstitial nephritis—from three to six months, and a year. It is usually attended with œdema, or general dropsy. Effusion into the pulmonary tissue occasions urgency of breathing, and may lead to purulent pneumonia. Gangrene of the œdematous parts is often a troublesome complication. The amount of urine passed is considerably below the normal standard; it is often turbid, depositing an abundant sediment, and contains tubes in great abundance. Micturition is frequent, disturbing in this manner the patient's sleep. This is probably due to the fact that the urine contains, in this case, intermediate compounds which irritate the bladder; besides, it is seldom below the specific gravity of health. Uræmic symptoms are less frequent than in the interstitial nephritis, though I have recently witnessed violent uræmic convulsions in a marked case of parenchymatous nephritis in a patient 25 years of age.

The amount of uric acid in the urine does not seem to undergo any modification. The quantity of albumen, on the other hand, which the urine contains is very large, as much as from 15 to 20 grains of albumen being thus eliminated in 24 hours.

Patients thus affected become cachectic and anæmic very suddenly. Cardiac hypertrophy, cerebral hæmorrhage, and albuminuric retinitis are not usual in the early stages of the disease, but may occur in the later. The patients may temporarily be restored to comparatively good health, even after violent uræmic convulsions, as in the case just alluded to. Patients may live from five to six and ten years, and it is in these cases that the small white granular kidney is found.

The interstitial variety of nephritis is more especially a disease of advanced years, and due most frequently to gouty diathesis, alcoholism, over-eating, &c. I have seen a case, however, quite recently, in a man of 34 years of age. A large quantity of pale urine, of low specific gravity, is passed; and *usually* the quantity of albumen in the urine is not so large as in the parenchymatous variety, and it contains a smaller number of tube casts. In the latter case referred to, the urine was *loaded* with albumen, and contained a considerable variety of hyaline tube casts, coincidently with the characteristic symptoms of cardiac hypertrophy, atheromatous condition of the blood-vessels, pulmonary œdema and hæmoptysis, an exophthalmic appearance of the eye, and albuminuric retinitis with impaired vision, and uræmic tremblings, not, however, amounting to distinct fits.

In the *earlier stages* of the disease dropsy is unfrequent; habitual dyspepsia is complained of, due doubtless to blood poisoning—a fact indicated by the urea and carbonate of ammonia contained in the vomited matters. The patients are usually fretful, disturbed cerebral circulation doubtless accounting for this occurrence. Epistaxis is noted in many cases;

and there is sometimes an extreme itching of the skin, which has probably some connection with the cutaneous elimination of urinary products. The skin is sometimes covered with a white powder. Hæmatemesis is not unfrequent; and West has observed in female patients uterine hæmorrhages. Apoplexy may occur from the high arterial pressure.

Uræmic diarrhœa is not unusual. Patients are more prone to contract other diseases, such as bronchitis and pericarditis. Another accompaniment of interstitial nephritis is the co-existence of interstitial inflammations in other organs; for instance, in the liver, spleen, and stomach.

Of the amyloid kidney the indications are more equivocal. In slowness of evolution, usual absence of œdema, and character of the urine, the symptoms are similar to those of the cirrhotic kidney; but the patients have usually a peculiar cachectic appearance, while concomitant diseases of the liver and intestines generally exist. Hæmorrhages, hypertrophy of the heart, and uræmia are comparatively rare in this form of nephritis.

Dr. Noel Guéneau de Mussy *(Union Medicale)* remarks, that in cases of what he terms "latent albuminuria," albuminuria developes itself slowly, and is accompanied neither by anasarca nor by derangements of vision. Often its existence is overlooked until irremediable.

Slight albuminuria may exist for years without causing severe affection of the health. Latent albuminuria, like diabetes, is in many cases the expression of an arthritic dyscrasia, and is often preceded by uric gravel. Urate of soda is found in the tubuli, in such cases, and the secretory cells are atrophied.

Dropsy following intermittent fever is of two kinds: the one depends on pathological changes in the kidney, and the urine is more or less albuminous; in the other the urine does not contain albumen, and no satisfactory reason of its absence has been given. It is usually curable by quinine and other febrifuges.

Of the dropsy which occurs in leucocythæmia explanation has already been given.

Albuminous Urine from other Causes.

It has been sufficiently indicated in the foregoing that a standard relationship must exist between the various constituents of the blood, in order that it may be capable of the performance of its normal functions. We have seen that serous effusions are determined by physical as well as physiological conditions, the former comprising arterial tension in what manner soever induced, the latter perverted functional correlation of the living tissues owing to excess or diminution of one or more of the elements of healthy blood. The blood tension may be general, or local. If water be injected into the blood to an extent beyond the standard of health, vascular tension is induced, the globules of the blood probably undergo solution to some extent, there is a proneness to effusion of serum, and albumen appears coincidently in the urine. But these sequences do not specially depend on the *injection of fluid into the veins, as the same results are brought about by the ingestion of large quantities of water.* So much for general blood tension. Should the blood tension be simply local, as by obstruction to the return of venous blood from the kidney in nephritis, albumen also appears in the urine. We have

dismissed the consideration of nephritis in this relation. Paramount in importance among the causes of local vascular tension comes pregnancy; and this condition seems to operate in the manner indicated, by pressure of the gravid uterus on the iliac veins, or on the inferior vena cava. In addition to this purely physical cause, it must be remembered that the changed condition of the blood during gestation may also account to some extent for this phenomenon. It is noteworthy, according to Braun of Vienna, that puerperal convulsions occur in the proportion of 80 per cent. in primipera, and this he reasonably accounts for by the resistance offered by the abdominal walls to the distended uterus, and the consequent greater pressure on the kidney—a pressure so great that not only albumen, but fibrine and blood have been found in the uriniferous tubes. The same authority makes the sagacious observation, that when puerperal convulsions occur in the multipera, there is usually a multiple conception, a vicious conformation of the pelvis, an excess of amniotic fluid, or an unusually large fœtus.

The same condition may be artificially produced by ligaturing the renal vein of an animal.

Static congestion of the kidney, as from affections of the heart, liver, lungs, asphyxia, &c., act in the same manner; so also embolism, typhoid fever, cholera, diphtheria, and exanthematous fevers, in all of which the constitution of the blood undergoes change.

Local renal congestion and albuminuria may further be occasioned by the direct irritation and inflammation consequent on the administration of toxic proportions of certain medicinal agents. This is most marked possibly in the case of cantharides, either administered

internally, or consequent on the external application of fly blisters.* According to Gubler and Martin-Damourette the cantharidine is neutralised in the blood by the albumen, or alcaline bases, and acts only as an irritant when it is being liberated in the kidney with the acid urine.

In certain cases of cantharidine poisoning the cellules of the uriniferous tubes are found tumified, or to have undergone a granulo-fatty degeneration, while tube casts are found in the urine during life; in others blood globules, fibrine, and even vesical epithelium may be discovered.

According to Ollivier,† lead acts similarly both on human beings and on the lower animals; and in like manner ammonia (Potan), sulphuric acid (Leyden and Munck), chloroform (Ranke), nitric acid (Lehmann), phosphorus (Koch, Lewin, &c.), arsenic, mercury, alcohol, and silver.

Finally, albumen may appear in the urine from indulgence in certain articles of diet, notably eggs; and in cases of albuminuria the amount of albumen in the urine is markedly augmented after a nitrogenous diet.

Tests for Albumen in the Urine.

1. Whenever the urine contains any substance coagulable by heat and by nitric acid, and *not* precipitable by acetic acid, that material may be affirmed to be albumen, for we know of no other substance which presents these characteristics.

2. The albumen so distinguished may be derived

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* M. M. Bouilland, Morel-Lavallée, Rayer and Dourif.
† De l'Albuminurie Saturnine, Archiv. Med. 1863.

from the blood (a) without other blood elements, (b) with other blood elements, (c) from pus, (d) from chylous urine.

3. The presence of blood is proved by microscopical examination; but frequently the blood corpuscles do not present their characteristic appearance. If the urine be acid, they retain their appearance for a long time, being only a little jagged at their borders; more frequently they are distended, and of a spherical form. Their colour is lighter than usual, they present a sufficiently well-defined outline, but they do not adhere in the usual manner. If urine containing blood be allowed to stand in a conical glass, the blood deposits, and may be recognised by the naked eye. If the sediment be filtered from the supernatant fluid, the latter is found to contain albumen. But if the microscope should fail to reveal the presence of blood, chemical tests must be resorted to. Should the blood corpuscles be dissolved, they give to the urine a reddish-brown colour. If acetic acid be added to such urine, and the whole heated, a reddish-brown coagulum is obtained, which, on drying, becomes almost black. If this coagulum be dried, powdered, and treated with alcohol containing sulphuric acid, the fluid becomes reddish or reddish-brown, owing to the presence of hæmatin; and if the mixture be evaporated, an ash is obtained which contains iron, whose presence may be demonstrated by appropriate tests. In testing for hæmatin, Hiller boils the urine, and adds to it concentrated caustic potash. Any albumen which may have been precipitated is thus dissolved, and the fluid becomes of a bottle-green colour, owing to the formation of a ferrous hydrate. Further boiling causes a precipitation of the earthy phosphates, with which

precipitate the hæmatin is incorporated, yielding a reddish-brown or blood-red colour. The presence of pus is demonstrated likewise by microscopic examination, and by the addition of either liquor potassæ or ammonia, which causes the urine to become viscid and jelly-like. Chylous or fatty matter is recognised by the addition of sulphuric ether, whereby the urine is instantly rendered transparent.

4. If the urine be alkaline when it is voided, or neutral and become alkaline, it is not usually precipitable by heat, and the neutralisation of it by an acid does not necessarily impart to it this property.

5. If *a drop or two* of nitric acid be added to albuminous urine intentionally or accidentally, coagulation by heat is prevented; but the precipitation, with or without heat, is brought about by the further addition of nitric acid.

6. The mere precipitation of urine by heat does not necessarily indicate the presence of albumen, for the precipitate may consist of phosphates; hence, to eliminate this source of fallacy, it is necessary, *previous* to boiling, to add nitric acid, which dissolves the phosphates; or if nitric acid has not been so added, and if the precipitate be small, add a few drops of acetic acid, which dissolves phosphates, not nitric acid, which dissolves a light precipitate of albumen with equal facility.

7. Phosphoric acid, either in small or large quantity, does not cause opacity of the urine, but it prevents coagulability by heat.

8. Acetic acid does not precipitate albumen either in large or small quantity, and when little is used it *does not* prevent coagulability by heat; but in larger quantity the urine remains perfectly clear even at the point

of ebullition. In all these cases, however, the urine is coagulable by nitric acid.

9. Hydrochloric acid in small quantity does not precipitate albuminous urine, but it prevents its coagulability by heat.

10. Sulphuric acid, neither in small nor large quantity, precipitates albumen when the urine is cold. On being boiled it becomes opaque, but less so than if it contained no sulphuric acid.

11. Urine that is highly acid and free from extraneous intermixture is not always coagulable by heat. This, according to Bence Jones, happens when urine contains free hydrochloric or nitric acids in such quantity as to form a compound with the albumen, which is soluble both in cold and boiling water.

12. Nitric acid, added to concentrated urine, may cause a precipitate of nitrate of urea, but the microscopic appearances—even the naked eye appearances—are such as to obviate mistake. Or uric acid and urate of ammonia may be thus formed: The latter is dissolved in an excess of the nitric acid; not so the former—at least except with a large excess of acid. Here, again, appeal must be made to microscopic characteristics. But the urine may contain these salts in *common with albumen.* Then the presence and proportion of uric acid and urate of ammonia are determined by the addition of acetic acid, which does not precipitate the albumen; and by heating, the urate of ammonia is dissolved, and the albumen is coagulated.

13. Nitric acid in decomposing urates is apt to cause a formation of uric acid; the precipitate of uric acid disappears by heating; nitric acid by its oxidising in-

fluence may decompose and dissolve the albumen, and with heat a red colour is produced.

14. Nitric acid causes turbidity of urine containing turpentine, copaiba, cubebs, &c., but heat has no such influence.

15. Having guarded against all sources of fallacy, the most accurate test for albumen is the following:— Take a little concentrated nitric acid; into the urine to be tested, and contained in a test tube or champagne glass, let a little of the acid trickle down the side of the vessel. Admixture of the fluids does not instantly take place. The urine floats on the surface; the acid is underneath. Usually at the point of contact an intensely red, violet, or blue ring forms—the reaction of uroxanthine. Should the colour be *green*, bile pigment may be present; but if albumen, a circular and well-defined turbidity succeeds, and the flaky material gradually sinks to the bottom. Should the urine be also rich in urates, a turbidity (uric acid) may also be thus formed; but then the albuminous ring is lower than the one due to the urates, and separated from it by a clear ring, and the latter gradually vanishes towards the surface, while the former subsides. The application of heat, however, dispels all doubt.

Other tests, such as alcohol, corrosive sublimate, tannin, alum, and carbolic acid, have been used for the detection of albumen. Alcohol, it is true, causes an opacity of albuminous urine; but it has the same effect on urine containing mucus. Besides, alcohol thus added has a greater affinity for the water than for the salts in the urine, and the latter are thus precipitated.

Tannin not only precipitates albumen, but likewise mucus and other constituents of the urine.

Corrosive sublimate, in like manner, seldom fails to precipitate urine whether it contains albumen or not, being decomposed by the sulphates, phosphates, and the organic matters of the urine.

Alum is likewise, and for similar reasons, untrustworthy for the detection of albumen.

Tidy's test consists of equal parts of carbolic and acetic acids. I am not aware that it possesses any special advantages over the ordinary tests in common use.

Dr. Brown-Séquard *(Archiv. of Scient. and Pract. Med.)*, in referring to the fact that, while in certain cases, heat alone will not cause the coagulation of albuminous urine, and that in the majority of such cases the reapplication of heat after nitric acid causes a precipitate of albumen, infers that in such cases there must be a modification of albumen, which, so far from being coagulated by heat, actually is deprived of its coagulability by boiling.

In cases of purpura, albumen is sometimes found in the urine; but here, unlike what obtains in chronic nephritis, the proportion of urea and of salts is either natural or *greater* than in health.

In many other acute diseases albumen may be occasionally found in the urine; for example, in acute rheumatism, peritonitis, and typhoid fever, more especially when the diarrhœa is profuse. The albumen, however, in these cases is far from being so abundant as in chronic nephritis.

When urine contains much mucus, and is only slightly albuminous, and this coincides with the existence of pain in the track of the ureters, extending to the kidneys, this may be usually ascribed to acute in-

flammation of the mucous membrane of the calyces, of the pelvis, or of the ureter (pyelitis), and not to inflammation of the proper substance of the kidney. If the above should be complicated with nephritis, then dropsy is most ordinarily present.

Abscess of any portion of the urinary canal will cause purulent and albuminous urine. Microscopic examination will reveal pus globules, and alkalies give their characteristic reaction.

Urine containing semen is occasionally rendered opaque by the application of heat and nitric acid, like urine slightly albuminous. The microscope will reveal the presence of seminal animalcules, whose appearances are characteristic.

LECTURE VI.

Prognosis, as based on the extent of the Renal Inflammation, condition of the Urine, and Causes of Nephritis—Alcoholic Nephritis—The Relation of Albuminous Urine to Dropsy as bearing on Prognosis—Nephritis consequent on Scarlatina—Tube Casts in the Urine: their prognostic significance—Prognosis in Chronic Nephritis—Duration of Dropsy depending on Renal Disease—Tube Casts in Chronic Nephritis: the significance of their varieties—Disappearance of Dropsy: its effect on the Urinary Secretion—Concomitant Affections of other Organs. RETROSPECTIVE SUMMARY.—Ultimate Composition of the Living Body—Varieties of Cells—Centres of Nutrition—Secretory Cells—Excretory Cells—Properties of Cells—Healthy Blood; its Relation to Protoplasm—Normal Correlation of Cell and Tissue—Influence of the Nervous System on the Circulation of the Blood—Pathological Changes in the Kidney—Influence of Alcohol on Nutrition. TREATMENT OF NEPHRITIS.—Indications of Treatment—The so-called "Expectant Treatment"—Doctrine of "The Change of Type"—Bleeding in cases of Nephritis—Treatment of more Chronic Forms of Nephritis by alteratives—Counter-irritation—Diaphoretics—Employment of Diuretics—Employment of Diluents—Treatment of Anasarca, and Secondary Complications.

GENTLEMEN,—As a general rule, it may be laid down that in proportion to the vascularity of an organ, so are the chances of structural changes following inflammation, and the persistence thereof. Acute inflammation of the kidney is at all times an affection of considerable gravity. The gravity of the attack may be rationally estimated by the extent to which the function of the organ is interfered with, and this may reveal itself by departures from the quantity and quality of the fluid excreted. In general, then, if the amount of urine be considerable, the quantity of albumen contained in it small, the specific gravity not far from normal, if

there be few blood-globules—these constitute a favourable indication. Sometimes, though very rarely, cases in which the urine presents little variation from that of health terminate very abruptly in death, while cases in which the contrary condition exists terminate favourably.

But the state of the urine alone does not suffice in forming a prognosis; the condition of the various organs of the body must be examined, and due weight be accorded to the result of the examination.

The *cause* of the nephritis must also be taken into consideration. Mechanical albuminuria—static congestion of the kidney—as in the latter months of pregnancy, may be looked upon as the least serious of the various forms of albuminuria. That following scarlatina, if properly treated, is usually not serious. If death does not take place within the first fifteen days, a favourable prognosis may be entertained.

In the case of persons frequently exposed to cold and addicted to alcoholic indulgences, an unsuspected chronic nephritis may take on the symptoms of an acute nephritis. The prognosis in such a case would be correspondingly grave.

The persistence of albumen in the urine after the disappearance of dropsy is an unfavourable sign; an acute attack frequently supervenes, which ends in intractable structural changes.

Should the nephritis be due to an exposure to causes which have been removed or combated by treatment, and the albumen gradually disappear, and the dropsy disappear in a corresponding manner, a favourable termination may be predicted. Exceptions to this, as to all other rules, must be held as possible. Nephritis consequent on scarlatina, if promptly recognised and

appropriately treated, terminates favourably in the majority of instances.

From what has been already advanced it will be obvious that the presence or absence of tube casts, their nature, and the condition and quantity of the urine, must receive attention likewise.

The prognosis in cases of *chronic nephritis* is of the greatest gravity. The termination of the vast majority of such cases is unfortunately in death. The duration of the affection will depend on the gravity and extent to which the functional derangement of the kidney exists. Hence, if the quantity of albumen passed in the urine be small, capable of being restrained by medicinal agents, or the loss compensated by careful and appropriate regimen, if dropsy be inconsiderable, or have disappeared, if the urine approach its normal specific gravity, and if there be no complication of internal organs, the patient may live a long time, even with considerable structural disorganisation of the kidney.

Dr. Gregory mentions the case of a man who suffered from dropsy depending on renal disease for the long period of *thirty years*. On admission into hospital the urine was found highly coagulable; its specific gravity was 1020, and but 12 ounces were voided during the twenty-four hours. Eleven days afterwards the quantity secreted amounted to 24 ounces, its specific gravity amounted to 1018, and contained no albumen. During the patient's stay in hospital the amelioration in his condition was very striking.

In *chronic nephritis* the size and nature of the tube casts are of weighty significance relatively to prognosis. Large granular and large hyaline casts indicate, as we have seen, an advanced condition of renal degeneration,

that contraction of the kidney is proceeding; and the greater the number of large tubes, so may the rate at which structural changes are proceeding be estimated.

In direct proportion to the size and number of tube casts, so likewise will the specific gravity of the urine be found to be diminished, and its contained albumen augmented.

The greater the quantity of albumen in the urine, the greater the gravity of the case. Dr. Christison, however, thinks that the contrary obtains.

Fatty tube casts, with fat cells in the urine, indicate advanced disease; yet recovery has taken place even in cases thus far advanced. Dr. Johnson has seen recovery in cases where fat cells had existed in the urine continuously for many weeks, and after albuminuria had existed for two or three years. The same authority relates the case of a medical man who suffered from albuminuria, more or less, for thirty years.

A marked augmentation of urine often coincides with the disappearance of dropsy and the diminution of albumen in the urine. Occurring in the comparatively early stages, this must be regarded as a favourable sign; but in later stages an augmentation of the urinary secretion indicates rather advanced desquamation of the tubes, and is of correspondingly serious augury. Fatal cerebral symptoms are often preceded by a diminution or complete suspension of the urinary secretion.

Concomitant affections of other organs will necessarily complicate and add to the gravity of chronic nephritis.

Retrospective Summary.—In ultimate composition living animal structure consists of minute bodies, termed

molecules of organisation, and are divisible into three kinds—nitrogenous, fatty, and mineral.

From these molecules are formed cells, through whose agency, and by properties peculiar to them in the vegetable as well as in the animal kingdom, are effected what are termed the organic processes—viz., those of secretion, assimilation, and excretion.

By a cell is understood a spheroidal body, having a wall or envelope, and containing material termed protoplasm, which may be regarded as the structural unit of the organism. In the higher organisms each cell contains a round central body, termed a *nucleus*. At the bottom of the animal scale, however, all the phenomena of life are exhibited by masses of protoplasm containing no nucleus.

Cells may be divided into (1) *Centres of nutrition*, which are merely nucleated cells, from the nucleus of which successive broods of young cells are developed. The function of a germinal centre is to withdraw from the blood material of nutrition for the repair and construction of the special organ or texture in which it may be situated. The original centre of nutrition—that from which the whole organism is formed—is the germinal spot of the ovum. (2) *Secretory Cells*. It is the function of the secretory cell to elaborate a new compound required for ulterior purposes in the economy; for instance, to facilitate assimilation, digestion, or locomotion. (3) The *Excretory cells*. This variety differs from the former in that their function consists in the removal of effete and useless material—material which, if retained, would react upon the system as a poison.

All cells are separated from the blood simply by the interposition of a thin membrane.

Each cell possesses special properties, according to the gland or structure in which it is situated. Thus, while no structural peculiarity is recognisable, the liver cell secretes bile, that of the sublingual and submaxillary glands saliva, and that of the mamma milk.

Secretion appears to take place between the nucleus and cell wall, and is evidently the product of the nucleus.

Cells possess three essential properties—viz., those of vital selection—whereby each cell appropriates according to its special wants,—osmosis, and chemical combination.

To produce healthy structure to replace the waste of tissue, the protoplasm supplied to the germinal centre must be suitable or pure, and this will depend on the condition of the blood from which it is derived.

Given healthy blood, healthy protoplasm is elaborated by the germinal centre, and healthy tissue to replace that which has become effete, and is being converted into ultimate products by oxidation.

In order, likewise, that secretion and excretion be normal, the blood supplied to the secretory and excretory cells must, in like manner, be healthy. Otherwise perverted chemical combination ensues, leading to structural changes in the cell and ultimate disorganisation of the organ.

The normal correlation of cell and blood may be disturbed in a twofold manner. In the first place, the blood may be healthy, but its supply may be deranged; hence disordered circulation even of pure blood may induce mal-nutrition, mal-secretion, and mal-excretion. In this case the property of *osmosis* possessed by the cell is the first to suffer. In the second place, perverted cor-

relation of cell relatively to the blood may be primarily due to blood impurity, leading, however, in like manner, to ultimate disorganisation in consequence of abnormal *chemical* changes.

The circulation of the blood is under the influence of the nervous system. The motor system carries on the circulation; the sympathetic regulates the tonicity of the minute arterioles. Section of the sympathetic, or transient impressions exercising a paralysing influence upon it, is followed by congestion of the particular organ or structure to which the portion of the nerve so influenced is supplied. Hence the influence of cold upon the loins, by acting upon the splanchnic nerves, may induce simple nephritis, which may, of course, proceed to ulterior pathological changes, ending in destruction of the kidney and death. (*Vide* pages 29 and 30.)

The pathological changes which the kidney undergoes in chronic nephritis may, in general terms, be said to be either inflammatory, purulent, lardaceous, or fatty. The inflammatory consist in congestions and effusion of coagulable lymph, with contraction; the fatty, in degeneration (*vide* page 68) of the protoplasm of the cells and structure of the kidney. Due oxidation of tissue, we have seen, is essential to healthy repair and secretion. Decarbonised blood will effect retrograde changes of tissue, resulting in the formation of fat. Alcohol is a hydrocarbon; excessive indulgence in it causes the blood to be surcharged with carbon—an effect striking enough in the appearance of the habitual drunkard. Hence observation and experience abundantly prove, that amongst the most frequent causes of chronic nephritis and cirrhosis is recognised chronic alcoholism.

Treatment.—In the treatment of inflammation of any portion of the body the indications will vary according to the stage of the disease, and consequently the period at which the patient comes under observation. If it be the initial stage that we are called to treat, we attempt to remove the cause, relieve local congestion, and thus restore the normal circulation and function of the part. Should the disease have passed into the secondary stage —viz., that of effusion,—in addition to the foregoing, we endeavour to stimulate the absorption of the effused products. If evidences of structural changes exist, and if the function of the organ be impaired, endeavours must be directed with a view to repair, and of imposing vicarious duty on other organs.

There is perhaps no disease in which the fashionable waiting-upon-death of modern physicians is more to be reprehended than in the treatment of acute nephritis. If the history of the case furnish, as a presumable cause of the affection, an exposure to cold or damp—and the latter you frequently observe at this hospital, in this relation, in the cases of miners, who present themselves suffering from anasarca, which they are unable to account for,—I say, if there be a history of exposure to cold or damp, with albuminous urine, with or without the other indications of nephritis, general bleeding should at once be resorted to. It is perhaps the most potent means of fulfilling the indications which the first stage of inflammation furnishes. The quantity of blood removed ought to bear a proportion to the intensity of the febrile disturbance and the suddenness of the accession of dropsical symptoms.

That general bleeding has done good in these cases the testimony of competent and reliable physicians

abundantly proves, and that it will and ought to do good, reason teaches us to believe. The reaction against general bleeding limits us to one of two conclusions: either Nature cured inflammatory affections in times gone by, and the testimony and observation of the writers of these times are worthless, or the diseases of the one age are not curable by the means adopted in the other. To evade this peculiar dilemma the doctrine of change of type has been propounded—a doctrine I have no hesitation in pronouncing one of the most melancholy that could be advanced to flatter conceit, palliate scientific imperfection, and condone a contemptible subserviency to the caprice of fashion.

Nature's laws may change, but man's judgment, never!

The blood, we have seen, in acute nephritis, is surcharged with fibrine, and effusion of fibrine into the inflamed organ is one of the complications especially to be guarded against. General bleeding, it is well known, diminishes the amount of fibrine in the blood.

Should the symptoms be less severe, cupping over the region of the kidneys may take the place of bleeding; or after venesection may have been practised, the withdrawal of blood by means of cupping may follow, according to the indications of severity.

Should these methods be deemed too severe, blood may be withdrawn by means of leeches applied to the loins.

In either case the bleeding may be subsequently encouraged by the application of large linseed meal poultices, which may be advantageously covered or mixed with laudanum, or by hot fomentations applied to the loins. The poultices or fomentations should not be

permitted to become cold, but should be repeated on the slightest fall of temperature. An excellent method of applying heat, with a regulated temperature, is supplied by the india-rubber bags suggested by Dr. Robertson, of the Town's Hospital, Glasgow. Alternately with these measures hot water baths should be employed. A feeling of oppression or faintness sometimes induced in this manner is to be guarded against. The skin should be carefully dried after the bath, the patient replaced in bed well covered, and the action of the skin encouraged by small doses of antimonial or ipecacuan wine, frequently repeated, or small doses of compound ipecacuan powder; or James's powder may be substituted, or alternated with the former. Under all circumstances, exposure to change of temperature must be scrupulously guarded against. These are the methods by which congestion of the inflamed kidney is most likely to be relieved.

But should the patient not have been treated in the earliest stage—a circumstance indeed of the most frequent occurrence,—in addition to the renal congestion there exists more or less effusion of coagulable lymph; this we endeavour to get rid of by stimulating absorption. Of all the remedies that stimulate the absorbents, none possess that property in a more marked degree than the preparations of iodine and mercury. Furthermore, mercury fulfils another important indication in the treatment of nephritis—it diminishes the amount of fibrine in the blood. And why should mercury diminish the amount of fibrine in the blood? It stimulates the function of the liver; and we know that fibrine is lost to the blood in passing through the liver, its nitrogen combining, as we have seen, with lower

products of oxidation to produce urea. The more active the function of the liver the greater consequently will be the destruction of fibrine, and the amount of urea formed. In cases of nephritis, I am bound to tell you that with the vast majority of practitioners mercury is a drug tabooed. That it should be so I believe to be one of the many beliefs current among medical men, unfounded on reason, and contrary to the experience of competent observers. If you ask why, if mercury has a beneficial effect in other inflammatory affections, it should not have an equally beneficial effect in nephritis, you are simply informed that in these cases it speedily causes salivation. I am not disposed to assent even to the truth of the objection; but even assuming it to be true, I answer that salivation is not a serious disease, and it certainly accords with my experience that the administration of mercury has mitigated the most alarming symptoms of nephritis, if it had not actually cured the disease. In the hospital I have given the bichloride of mercury in small doses, 1-16th of a grain, combined with iodide of potassium—a biniodide of mercury soluble in excess of iod. potass. being thus formed—and have satisfied myself that the quantity of albumen in the urine was thereby diminished. In cases of syphilitic cachexia its special indication will be too obvious to necessitate comment.

Recently I saw at the dispensary a boy suffering from nephritis with anasarca, consequent on scarlatina. Grey powder in two grain doses, with one grain of ipecacuanha, night and morning, were prescribed. Œdema of the face had taken place to such an extent that the boy could not see, being unable to open his eyes. There was also very great dyspnœa. I afterwards saw

patient in private. Exposure to cold had evidently aggravated his condition, as pulmonary œdema had supervened. The treatment was persevered with, with the addition of antimonial wine and liq. ammon. acet., and the boy made a good recovery. In similar cases I would certainly advise grey powder and ipecacuanha, in addition to the treatment already referred to.

Against the use of opium in any form you must be specially on your guard. It causes increased congestion of the kidney, diminishes the secretion of urine, and may thus speedily induce coma, or other uræmic symptoms.

Analogous to mercury, in its action on the absorbents, is iodide of potassium; and it has long enjoyed, especially among continental physicians, a high reputation in the treatment of nephritis. Prudente, and after him Semmola of Naples,* attributed to it a marked influence in arresting renal degeneration. Crocq† has advocated its employment in even stronger terms. He contends that the dose should be large, and that in these cases there is a marked toleration of the drug. He advises the combination with iodide of potassium, of iodide and perchloride of iron, with tannin.

It is well to bear in mind that not unfrequeutly evidently the worst cases recover, while apparently slight ones unexpectedly and suddenly terminate fatally.

In the more advanced stages of nephritis counter-irritation should be applied over the region of the kidney. As to the nature of the counter-irritant difference of opinion may exist. Cantharides has been objected to from a dread of its causing strangury, and conse-

* Bulletin Gén. de Thérap., t. lxiii.

† Trait. de la Néphrite (Bull. Thérap., t. lxiii.)

quently doing mischief; but in view of the fact that tincture of cantharides has itself been employed in the treatment of chronic nephritis, the objection should carry less weight. Rayer testifies to its good effects, though he remarks, "C'est un remède incertain et qui pourrait être dangereux dans des mains inexpérimentées." I should certainly regard it as not only a dangerous remedy, but one whose *modus medendi* would seem to me perfectly inexplicable.

Should the application of cantharides to the loins be dreaded, counter-irritation may be established by tartar emetic ointment, croton-oil, iodine, &c.; and while the skin is tender mercurial or iodine ointment should be judiciously applied.

Instead of the ordinary counter-irritation, the actual cautery may be applied, or setons may be established for a like purpose. With a view to vicarious elimination of urinary constituents, the bowels and skin should be acted upon. On no account would I advise you to have recourse to saline purgatives, for a considerable portion of the salines are eliminated by the kidney. Medicines which are eliminated specially by the bowels are therefore to be preferred. Elaterium may be given in doses of from $\frac{1}{4}$ to $\frac{1}{2}$ a grain in combination with colocynth pill mass, combined, should there be no contra-indications, with a little mass. pil. hydrarg.; scammony, gamboge, and castor-oil may also be beneficially employed.

The skin is best acted upon by baths, antimonials, and liq. ammon. acet.

Diuretics are actually employed at the present day*

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* This practice is inculcated at a certain Scotch University. A learned

in the treatment of acute and chronic nephritis—on what basis in reason, or common sense, I have ever failed to comprehend. I have always regarded it as an axiom in the treatment of inflammation, that rest to the inflamed organ is of the first importance. As well, in my opinion, command a man suffering from double pneumonia to leave his bed and take a three mile race, as give stimulating diuretics in a case of nephritis. Those diuretics *do act as such*, by causing transient congestion; and how they can act favourably in nephritis may well tax the fertility of the most luxuriant imagination.

The administration of diluents in albuminous nephritis is strongly recommended by certain authorities. Dr. Geo. Johnson particularly insists on this line of treatment. Referring to the treatment of acute Bright's disease, he remarks, "In a large proportion of cases, rest in bed, with a scanty diet, and *a liberal use of diluent drinks, will suffice for the cure.*" You will agree with me, I have no doubt, in the difficulty of reconciling such treatment with the facts, that the ingestion of large quantities of fluid increases the vascular tension, that whatever increases blood tension causes an augmentation of albumen in the urine, and the indisputable clinical observation, that *in proportion as fluids are withheld in cases of albuminous nephritis, so is the amount of albumen in the urine diminished.* This fact seems not to have escaped the notice of Dr. Johnson, though he has failed to recognise its importance in the treatment of

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Professor (perhaps the best theorist in Europe), in recommending the bitartrate of potash in cases of this nature, terms it a "double-barrelled weapon"—it will kill or cure? I scarcely think the analogy goes far enough. In view of its killing properties, I think it might be designated a "*breech-loader!*"

the disease, for he remarks, "Let me impress upon you one point of practical importance. Before you pronounce a patient to be entirely free from his malady, be careful to test the urine, not only after rest and fasting—*i.e.*, in the morning before breakfast,—but after food and exercise. Albuminous urine is usually more copiously so after food and exercise; and you will sometimes find that, while the urine before breakfast is quite free from albumen, that which is secreted after a meal is decidedly and even copiously albuminous." And why should this be so? Because blood pressure is thus increased by fluids partaken of, while nitrogenous diet largely indulged in likewise determines increased albuminuria *(vide* page 122). I would therefore warn you to be cautious in your use of diluents in albuminous nephritis.

Scarifications of anasarcous parts are, as a rule, not to be advised. I have frequently seen diffuse erysipelatous inflammation to supervene in consequence. The application of blisters for the removal of serum is a practice still more to be reprehended. What more likely than that an intractable slough should follow the application of a blister to a part with such depressed vitality?

Secondary affections must be treated on general principles. The diet of the patient should be of a nutritious description, consisting of animal food, milk, &c. Alcoholic drinks should be strictly forbidden.

Notwithstanding your utmost endeavours, nephritis will prove of the greatest gravity; but you will be acting worthily of your profession and of your duty to society, by treating this and all other diseases on the general principles of our art established by time, talent,

and the experience of our predecessors, to the extent that these harmonise with your mature judgments—contemning alike the influence of mere fashion, and the sacrifices that a manly adherence to truth always entails.

WORKS BY THE SAME AUTHOR.

Observations on Therapeutics and

Disease. 8vo.: Price 2s. 6d. London: J. & A. Churchill.

"Dr. Black is one of those thinkers who ought to be encouraged, . . . we have said that we think such an attempt as Dr. Black's is one to be encouraged. We think so because boldness of thought, and a disposition to handle the problems of disease and of health in a large spirit, are very necessary to that great reform in therapeutics which we all hope to see. There is much ability in his pamphlet, and it will be an immense gain to practical medicine if he succeeds in stirring up our scientific therepeutics to look at questions of medication in a broad way, and in relation to the great physiological states, instead of merely ticketing remedies with specific titles, and inducing the hapless practitioner to discharge them at a supposed peccant organ, as a boy might aim a pea from a pop-gun."—*Practitioner.*

"Dr. Black's essay displays an extensive knowledge of his subject, and though many of his views are necessarily open to controversy, they are well worth consideration."—*Brit. and For. Med. Chir. Rev.*

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On the Functional Diseases of the

Urinary and Reproductive Organs. 8vo.: 2nd Edition: 10s. 6d. J. & A. Churchill, London: Lindsay & Blakiston, Philadelphia.

"This volume—the expansion as its author tells us of a proposed article for *The British Medical Journal*—is evidently written by a gentleman of considerable practical experience, deep thought, and extensive reading. The work begins with a disquisition upon the conditions affecting the secretion of urine, with special reference to suppression, in which those all important bases of exact medical science, the pathology and morbid anatomy of disease, are by no means neglected. Following this part, about seventy pages are devoted to a review of the varieties, causes, and management of retention of the urine after its secretion; and the remainder of the book is chiefly occupied with excellent investigations upon the pathology and treatment of nocturnal enuresis, spermatic incontinence and the allied subjects of masculine impotence and sterility, all of which the author most judiciously maintains, have been quite long enough abandoned by the regular profession to designing charlatans, who not only take advantage of the natural anxieties which assail sufferers from sexual disorders, but systematically aggravate the apprehensions of their victims from base pecuniary motives. The style of the author is easy and agreeable. . . . On the whole, his work is a valuable contribution to medical science, and being penned in that spirit of unprejudiced philosophical enquiry which should always guide a true physician admirably embodies the spirit of its opening quotation from Professor Huxley."—*Philadelphia Medical Times.*

"We like the tone of the book though it advocates many propositions not

accepted by the profession. Even these, we think will provoke discussion, nd so hasten the time when the functional diseases of the male shall be as carefully studied and treated as those of the female."—*Michigan Univ. Journal.*

"There is so much cleverness, *bon hommie*, and frankness, and apparent honesty of purpose, and distaste for quackery that hostile criticism is disarmed. . . . It is an interesting, original, and will probably prove a useful work. With Chapter IV. begins the real work of the Author, on "*The Pathology and Treatment of Nocturnal Enuresis and Spermatic Incontinence.* This is followed by a well-reasoned and manly discussion of the unsavory subject. The practical observations on treatment are sensible. The book is nicely got up and the Table of Contents and Index are admirably arranged." —*Edin. Med. Jour.*

"Dr. Black deserves all praise for the manliness, heartiness, honesty of purpose, and scientific zeal with which he has treated a subject which has become distasteful from its associations, which has been too much shunned by our profession, and which has unfortunately fallen almost altogether into the hands of charlatans. . . . Dr. Black's book contains much useful information, and will doubtless prove interesting to many readers."—*Birmingham Medical Review.*

"This is an important work, showing extensive research and conveying much information."—*The Doctor.*

"There are some points in reference to the functional disorders of the reproductive system that are continually forcing themselves upon medical men, but which few practitioners care to investigate. Some of these have been fully discussed in this and other medical journals, but unfortunately such topics are apt to be neglected, and hence fall into the hands of those least qualified to discuss them. Hence the continual increase of a class of literature that we cannot but condemn, and which finds its way into the hands of ignorant young men, who thus become the victims of quackery.

These topics require most careful handling by highly qualified men, and yet the majority dislike to associate their names with them, and even able writers on diseases of the generative organs frequently omit the consideration of those disorders that possess a real existence and feed the charlatans. It is desirable, therefore, that such writers should supply the omission, and thus prevent the subject from remaining in unqualified hands, and it is also well that medical journals have of late years directed attention to them.

We have had by us for a long time a volume by Dr. Campbell Black, in which the topics we have alluded to, are freely discussed, and which is, perhaps, the best work of reference respecting them for medical men."—*Med. Press and Circular.*

On Certain Aspects of Medical Reform.

On the Relations of Prescriber to Dispenser.

"Dr. Black speaking boldly on these and other subjects, we cordially wish him success in his efforts at medical reform."—*Westminster Review.*