Lectures on Bright's disease of the kidneys : delivered at the School of Medicine of Paris / by J.M. Charcot ; translated, with the permission of the author, by Henry B. Millard.

BRIGHT'S DISEASE OF THE KIDNEYS

CHARCOT

LECTURES

ON

BRIGHT'S DISEASE OF THE KIDNEYS

DELIVERED AT THE SCHOOL OF MEDICINE OF PARIS

BY

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TRANSLATED WITH THE PERMISSION OF THE AUTHOR,

BY

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ERRATA.

Page 18, line 31, for "afferent," *read* efferent.

Page 25, 12th line of the Summary, for "Hyalin," *read* Hyaline.

TRANSLATOR'S PREFACE.

I KNOW no work which, with such conciseness and precision, presents the various characteristics of the important disease which is the subject of these lectures as that which I have the honor of introducing to the American reader.

Much more voluminous treatises exist, it is true, upon this subject, but none, it seems to me, which give with so much clearness and well-chiselled outlines the salient and practical features of the disease.

No disorder of the kidneys is considered, with the exception of scarlatinous nephritis, but such as may be strictly included under the denomination of "Bright's disease."

Its comprehension and study are greatly facilitated by the reduction to three forms of the numerous and perplexing classifications, often contradictory, which exist amongst most authors.

I hope, therefore, as I believe, that the work will be of value to the medical scientist and practitioner, in the diagnosis and pathology of this important affection.

H. B. MILLARD.

NEW YORK, *September*, 1878.

AUTHOR'S PREFACE TO THE AMERICAN EDITION.

As my *confrère*, Dr. Millard, desires me to write a few words of introduction to his translation of my lectures on Bright's disease, I beg to say that although the work does not consider the subject of treatment, this latter is so intimately connected with a thorough knowledge of the pathology and histology of the disease as to be really indispensable to the successful treatment of it.

The vague and general views frequently entertained by practitioners concerning the forms and pathology of Bright's disease I believe, in many cases, to militate against their successful management of it.

I will simply express the hope that this little work may be of practical value to my professional brethren in America.

J. M. CHARCOT.

PARIS, *July*, 1878.

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LECTURES ON

BRIGHT'S DISEASE OF THE KIDNEYS.

LECTURE I.

NORMAL ANATOMY OF THE KIDNEY.

Summary:—Preliminary Observations.—Normal Anatomy of the Kidney.—General Description of the System of Uriniferous Tubules.—Structure of the Uriniferous Tubules.—Wall Peculiar to the Tubes.—Endothelial Layer.—Rodlike Epithelium of the Convoluted Tubes and Ascending Branch of Henle's Loop.—Tesselated Epithelium in Other Places.—Topographical Anatomy of the Kidney.—Longitudinal and Transverse Sections.—Lobular Disposition of the Kidney.

GENTLEMEN:

The anatomical history of Bright's disease has become, of late years, particularly interesting. The histological lesions which the kidneys undergo in this disease, have, in fact, been studied with more precision than formerly, and, above all, have received an interpretation calculated greatly to modify the opinions that are generally entertained.

It will become apparent to you, from the study of these lesions, that the varieties they present relate especially, in the majority of cases, not to successive stages, but to distinct *forms* of the malady.

Before entering upon this chapter, I think it necessary to place before you, in the beginning, the principal facts relative to the structure and functions of the kidney. Recent

works upon this subject have inflicted, indeed, a severe blow upon the classic descriptions. Concerning this I shall be obliged to enter into some details which may seem to you minute, but their importance will become manifest to you later; and I assure you that, to whomsoever wishes to enter thoroughly upon the investigation of the histological alterations of the kidneys, a knowledge of them is indispensable.

I.

I will commence this exposition with the description of the system of the uriniferous tubules (*tubuli uriniferi*). It may be stated, in a general way, that it is composed of a considerable number of tubes, all founded upon the same plan, each tube originating in an ampullary dilatation, which is situated in the cortical layer, and finally opens into the pelvis of the kidney by an orifice called the papilla; in the course, however, of this long journey it has undergone many important changes in diameter, direction, and even in structure, which it is important thoroughly to understand.

The name *Glomerulus Malpighi* is applied to a small and quite unique vascular apparatus contained in a membranous envelope, the *capsule of Bowman*. The cavity circumscribed by this membrane is really the termination, or rather origin, of each of the uriniferous tubes; the capsule opens, indeed, at an opposite point to that which gives access to the vessels of the glomerulus, by a tubular passage, straight at its commencement, called the *neck* of the capsule. This neck is continuous, with a sinuous canal larger than itself, in which occur a great part of the most important, or at least special phenomena of the renal secretion. These canals, relatively voluminous, and meriting, by the sinuosities they describe,

their name of *tubuli contorti*, are all, like the glomeruli, situated in the cortical layer of the kidney.

At a given moment the convoluted tubes undergo a progressive diminution in size, and give origin to a straight tube, which, without presenting in its course the slightest change in its calibre or the least sinuosity, descends straight down towards the papilla; this is the descending, or small branch, of Henle's loop. At a variable distance from the papilla, the tube bends abruptly upon itself, forming a short curve known as *Henle's loop*, and ascends parallel to the descending branch to the neighborhood of the renal capsule; this new portion is known as the *ascending*, or, rather, as the *large branch* of Henle's loop, inasmuch as, after having described the curve, the canal undergoes a new increase of calibre. The point at which this augmentation of the calibre takes place

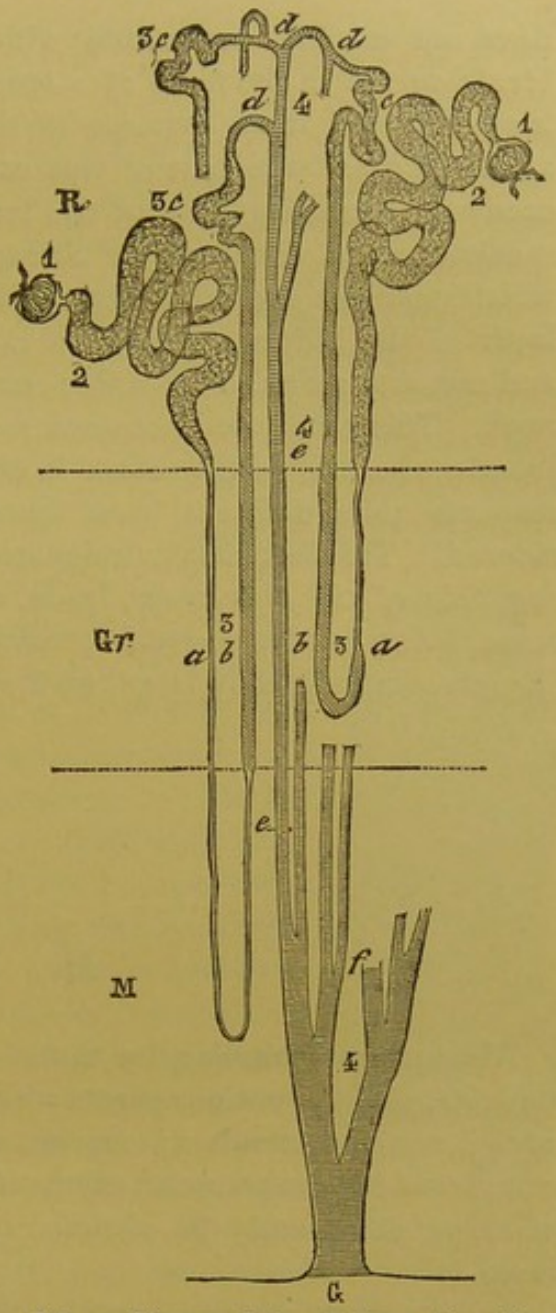

FIG. 1.—Diagram of the uriniferous tubes (after Schweigger-Seidel, *Die Nieren des Menschen und der Saügethiere*. Halle, 1865. Taf. IV., f. 1).

R, Cortical substance.

Gr, Zone of limitation.

M, Medullary substance.

1, Capsule of Bowman and glomerulus of Malpighi.

2, Convoluted tubes (*Tubuli contorti*).

3, *a*, Henle's loops, descending or small branch: *b*, Ascending or large branch. *c*, Intermediate piece.

4, Excretory tubes (straight tubes, tubes of Bellini). *d*, Junctional tubes. *e*, Collecting tubes of the first class. *f*, Collecting tubes, second class.

G, Papillary orifice.

does not exactly correspond with that where the canal of Henle curves in the form of a loop; sometimes, indeed, the loop is formed at the expense of the slender, and sometimes at that of the large part of this canal. The part which succeeds the ascending limb of the loop is known as the intermediate piece (*Schalstück*, Schweigger-Seidel); this part, which occupies the most superficial portions of the cortical layer of the kidney, presents a calibre comparatively large, and numerous sinuosities which recall those of the *tubuli contorti*. This canal soon becomes smaller, and constitutes the junctional canal, which unites itself with a conduit in many respects quite different from those we have hitherto considered. This last canal, designated by the name of *collecting tube of the first order*, leads, as do other canals of the same order, into larger trunks, which finally open by an orifice (the faveola) relatively large, at the summit of the papilla.[1]

II.

We are now familiar, by name and some of their characteristics, with the various pieces which enter into the formation of the uriniferous tubes; our knowledge must, however, be completed by a more exact study of the structure of each one of these parts and the various peculiarities presented by them.

I will not at present consider the Malpighian corpuscles,

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[1] Consult on the anatomy of the uriniferous tubes, Henle: *Handbuch der Systematischen Anatomie des Menschen.* 2d Bd., 2 Auf., 1st Lief. Braunschweig, 1873.—Schweigger-Seidel: *Die Nieren des Menschen.* Halle, 1865.—C. Ludwig: *Von der Niere.* Stricker's Handbuch, 1st Bd. Leipsic, 1871.—Ch. F. Gross: *Essai sur la structure microscopique du Rein.* Strasbourg, 1868.

and as to the capsule of Bowman, will simply say that it is formed by a membrane without apparent structure, upon the inner surface of which may be distinguished, especially after impregnations of silver, a complete endothelial layer. This endothelium is continuous with that which carpets the cavity of the neck of the capsule, but undergoes, at the point where the *tubuli contorti* commence, important modifications. Before, however, describing the character of the epithelium of the convoluted tubes, I should mention that in them, as in most of the uriniferous tubes, the walls of these canals seem to be formed by an anhistous membrane; although Mr. Ludwig affirms that he has found in these walls evident traces of a disposition which recalls that described by M. Debove[1] as existing in the basic membrane of certain portions of the intestine; according to it, the limiting membrane of the convoluted tubes is composed of flattened cells placed in juxtaposition, whose contours are made apparent by impregnations of silver.

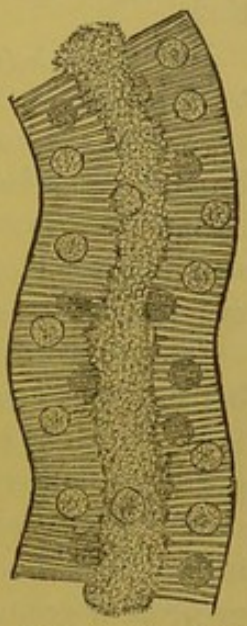

FIG. 2. — Convoluted tube with rod-like epithelium (after Heidenhain).

To the epithelium of the convoluted tubes, which is to a certain extent the fundamental element of the kidney, belong especial characteristics with which the recent researches of Mr. Heidenhain have made us familiar.[2] The cells which form this lining, as we know, almost coalesce; they are voluminous, and leave in the cavity of the tube only a narrow lumen; their nuclei are not easily apparent; they are, besides, naturally cloudy, and have a dull tint, a yellowish hue, that has been observed for a long time by all anatomists, which they account for by the existence of numerous granulations more

[1] Debove: *Mémoire sur la couche endothéliale sous-epithéliale des membranes muqueuses.* Arch. de Physiolog., 2e série, t. I., p. 19, pl. II. 1874.

[2] Heidenhain, *Mikrosc. Beiträge zur Anat. und Phys. der Nieren.* Schultze's Archiv für mikr. Anat., 10. Bd., 1874, S. I.

or less brilliant, some protein, the rest fatty. According to Mr. Heidenhain, on the contrary, these granulations are only the optical sections of a certain number of little rods occupying the body of the cell, imbedded as they are in the protoplasm, their direction being parallel to the transverse axis of the tube. This rod-like epithelium may be studied by the aid of great enlargements upon transverse or longitudinal sections of the tubuli contorti, in a kidney treated by the bichromate of ammonia, and afterwards by hæmatoxylin; the rods and nuclei are then colored blue, and placed in relief; they appear as parallel striæ when the cells are viewed from the side; when viewed in face, they are shown in projection, in the form of small circles or of granulations.

These rods occupy particularly the part of the cell which touches the basement membrane; it is there that the striæ are most pronounced, and on isolating a cell of the epithelium of the *tubuli contorti*, there is seen from the side of the lumen the protoplasm and a part of the nucleus, and from the side of the basement membrane, the rods which seem to terminate by free extremities.

The arrangement I have just described, and which I shall be able to demonstrate by the preparations made by Dr. Renault in the laboratory of Dr. Ranvier, seems to be the principal cause of the cloudy and granular appearance presented by the epithelium of the *tubuli contorti;* it does not, however, exclude the presence of a certain number of fatty or protein granulations, which seem to occupy even in normal conditions the body of the rods.

In the descending limb of Henle's loop the epithelium suddenly undergoes a profound modification; we there find only, indeed, a tesselated and clear epithelium, swollen only at the level of the nucleus, and entirely analogous to that presented by the blood-vessels; it is, in fact, extremely difficult to distinguish between a descending limb of Henle cut transversely, and a transverse section of a blood-vessel.

In the large or ascending branch of Henle's loop, the character of the epithelium is once more changed: the cells composing it again assume the features of those lining the convoluted tubes; a new change occurs in the intermediate piece (*Schalstück*), where the epithelium, sombre, granular, rod-like, gives place to a clear epithelium which approaches the cylindrical epithelium, being simply more flattened, (Schweigger-Seidel, Henle).

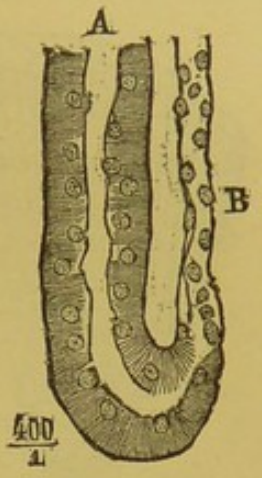

FIG. 3.—Loop of Henle (after Henle).
B. Descending limb.
A. Ascending branch.

Finally, the whole system of collecting tubes is lined equally by a clear epithelium. In the tubes of the first class, that is, in those nearest the capsule, the epithelium is flattened, and the cavity is proportionally very large; lower down, that is, in the largest collecting tubes, those approaching nearest the papilla, the lining is constituted by an elongated, cylindrical epithelium, perfectly developed.

Leaving now the individual study, in some sense abstract, of the uriniferous canals, we have next to observe the manner in which these canals are grouped, and combine to form the renal substance, and also what is the method of repartition of the various pieces of which they are formed, in the different regions of the kidney recognized by macroscopic anatomy.

Descriptive anatomy, as you know, distinguishes in the kidney two principal regions: one the region of the *cortical substance*, the other that of the *medullary substance*. The medullary substance, formed by the reunion of the *Malpighian pyramids*, may be in turn subdivided into two zones, namely: 1st, the papillary zone; 2d, the intermediate, or zone of limitation. The first is distinguished by a generally bright color, the second is striated lengthwise by a series of rays alternately pale and colored. The pale rays extend into the cortical substance in the form of small cones, whose

color is less pronounced than that of the neighboring parts; these are the *prolongations of Ferrein*, known also as *medullary rays* or prolongations (*Pyramidenforsätze* of Henle, *Markstrahlen* of Ludwig). The colored rays of the medullary substance continue without any distinct line of separation with the intermediate spaces to the medullary prolongations; the spaces, according to the nomenclature of Henle, being known as the cortical substance proper, and more simply, according to that of Ludwig, as the *labyrinth;* it is in the thickness of the labyrinth that the glomeruli of Malpighi and the tubuli contorti are found—that is, the real secreting portion of the kidney. I should add that the medullary rays do not extend upward entirely to the renal capsule; they are separated from it by a straight zone, which is only a prolongation of the substance of the labyrinth. You may follow all the details of this description in the diagrammatic representation that I have taken from Mr. Ludwig's work.

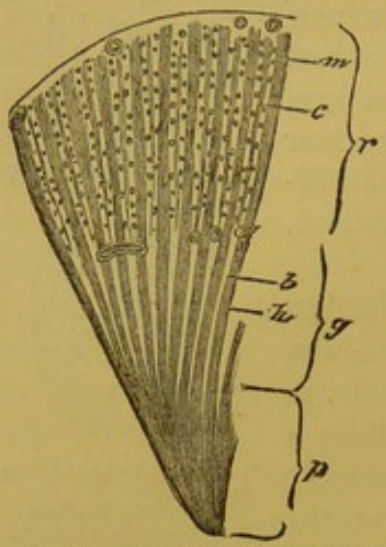

FIG. 4.—Horizontal section of kidney of a dog, in which the uriniferous tubes and blood-vessels have been injected (Ludwig in Stricker's Handbuch, Vol. I., p. 489, Fig. 138, English edition).

p, Papillary region.—*g*, Zone of limitation.—*r*, Cortical layer.—The dark striæ of the medullary substance (*h*) represent the fasciculi of the uriniferous tubes; they continue into the cortical substance, where they form the medullary rays.—The transparent portions (*b*), alternating with the preceding, correspond by their position to the vascular fasciculi of the zone of limitation.—The transparent portions of the cortical region, studded with small dark points (glomeruli, *c*), represent the labyrinth.

After this survey of the whole, we are in a position to ascertain what arrangement is presented by the different parts of the apparatus of the uriniferous canals in each one of the regions that have just been designated.

This study should be made successively upon longitudinal and upon transverse sections. It is very important for the researches of pathological histology that we should be familiar with the appearances presented by these various sections.

1. *Longitudinal sections.* — *A.* The *papillary region* is formed mostly by the collecting tubes which divide only in this region, and in part by a certain number of branches of

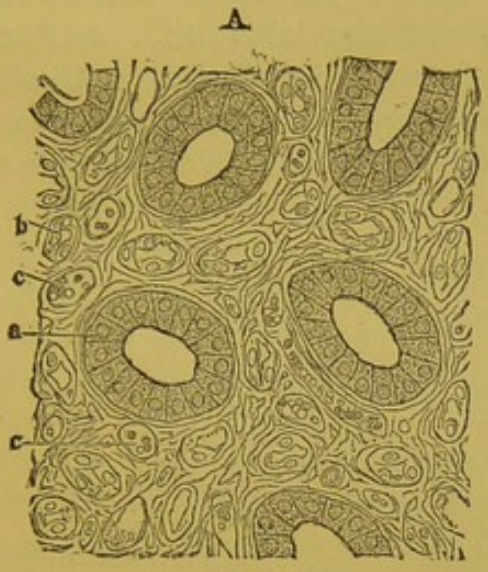

Fig. 5.

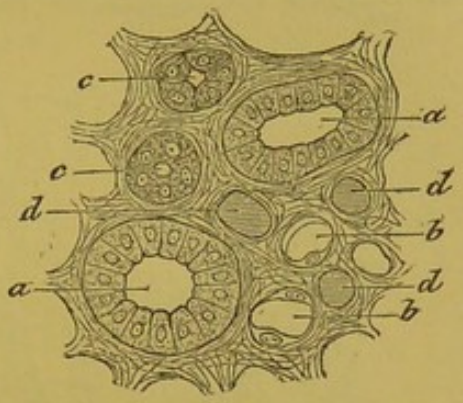

Fig. 6.

Fig. 5.—Transverse section of a renal papilla near the summit (Henle, Fig. 232 A).—*a*, Tube of Bellini.—*b*, Ascending branch of Henle's loop.—*c*, Blood-vessels.

Fig. 6.—Transverse section of the kidney at the level of the zone of limitation.—*a*, Collecting tubes.—*b*, Descending branch of Henle's loop.—*c*, Ascending branch of the same.—*d*, Blood-vessels.

Henle's loop formed at the expense of the slender tubes. There exist in this region only two varieties of uriniferous tubes.

B. In the zone of limitation, however, are found three varieties of tubes: 1st, the collecting tubes; 2d, the descending or small limbs of Henle's loop; 3d, the large or ascending branches of these loops. It is to the presence of these branches and to that of the blood-vessels, known by the name of *vasa recta*, that the augmentation of volume presented by the medullary substance in this region is due.

C. We find in the *cortical substance*, on sections made of the whole, proceeding from the surface of the kidney towards the hilum: 1st, the capsule of the kidney hollowed with lym-

phatic cavities or spaces; 2d, beneath this, a thin layer formed by sinuous canals, these being, especially at the pyramidal prolongations, intermediate pieces, and, in addition everywhere, convoluted tubes; 3d, deeper are found the prolongations of Ferrein and the labyrinth. *a*. The *prolongations of Ferrein* are formed: by the straight collecting tubes, by the large tubes or the ascending branches of Henle's loops, and, in addition, by the convoluted tubes

FIG. 7.—Antero-posterior section of cortical substance of kidney of an infant (Henle).—A, Prolongation of Ferrein.—B, Labyrinth.—C, Malpighian glomerulus.—D, Arterial branch.

which became transformed in the zone of limitation into the slender branches of Henle's loop. *b*. The region of the labyrinth contains in its centre the interlobular arteries whose lateral ramifications, like the branches of a tree, support upon their extremities the glomeruli of Malpighi; the convoluted tubes fill the entire space between the arterial ramifications and the medullary prolongations. The first view of the lobular texture of the kidney is afforded by a longitudinal section. Each *lobule* is represented in the cortical substance, upon the cut surface, by the region comprised between two interlobular arterial trunks. In the centre of

the lobule is seen the medullary prolongation; at the periphery, a zone formed by the contiguous parts of the labyrinth.

2. The *transverse sections* (perpendicular to the large axis of the pyramids) are not less instructive than the preceding.

A. Those made immediately beneath the capsule of the kidney expose only convoluted tubes and the intermediate pieces (*Schaltstück*); but deeper sections—towards the middle of the *cortical layer*, for example—show the renal lobule under a new aspect that it is important thoroughly to understand. *a*, At the limits of the lobule, the Malpighian bodies—their number being variable—are found; *b*, deeper, the labyrinth with the *tubuli contorti*; *c*, in the centre, finally, the transverse sections of the medullary rays, formed by the collecting tubes, recognizable by their cylindrical epithelium, flattened, in this region, and by the ascending limbs of the loops, characterized by a narrow lumen and cloudy epithelium.

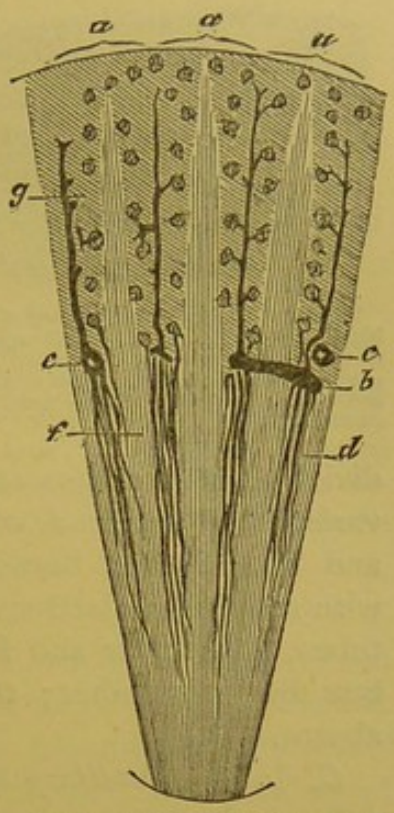

FIG. 8.—Diagram of the structure of the kidneys (after Rindfleisch, *Traité d'Histologie pathologique*, French translation, Fig. 189).—*a*, Bases of renal lobules presenting upon horizontal section (Fig. 9) polygonal figures.—*b*, One of the principal branches of the renal artery separating the medullary and cortical layers, and sending into the cortical layer ascending branches which bear the Malpighian bodies.—*c*, Renal veins.—*d*, Straight vessels.—*e*, Extremity of renal papilla.—*f*, Fascicles of straight uriniferous tubes, forming the pyramids of Ferrein of the cortical substance.

An exact knowledge of the lobular disposition presented by the kidney in the cortical zone is indispensable to the pathological anatomist (if he desires to mark its situation with reference to the cardinal points) in the researches of pathological histology; it is at the periphery of the lobule, as we shall soon demonstrate, in the region of the labyrinth, that are situated the most important lesions of the various

forms of interstitial or parenchymatous chronic nephritis—the anatomical substratum of Bright's disease.

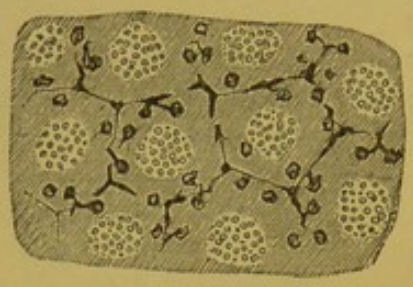

FIG. 9.—Diagram of the structure of the kidney (Rindfleisch). Horizontal section of the cortical substance. The renal lobules are shown under the aspect of polygonal figures; the interlobular vessels represent stellated figures.

B. Upon transverse sections made in the intermediate, or *zone of limitation*, in the vicinity of the cortical layer, an arrangement is observed, well represented in one of Henle's plates (pl. 239, p. 319, *loc. cit.*), and which recalls the lobular arrangement found in the cortical layer. At the periphery groups of vessels are found formed by the divisions of the vasa recta; the centre is occupied by two varieties of tubes: *a*, collecting tubes with clear epithelium; and *b*, ascending branches containing a cloudy epithelium with rod-like projections. Transverse sections of descending tubes, with clear and flattened epithelium, are also found, but few in number; the convoluted tubes are altogether absent.

C. In the *papillary zone* the cylindrical epithelium of the collecting tubes becomes longer, the relative number of descending tubes of the loop augments progressively, and, at a certain moment with the collecting tubes, are the only ones remaining, the ascending tubes having completely disappeared.

D. Finally, exactly at the level of the papilla, the collecting tubes only are found; they are devoid, at this point, of any proper wall, and the epithelium is there directly in contact with the conjunctive tissue (*Figs. 6 and 7*).

LECTURE II.

NORMAL ANATOMY OF THE KIDNEY (*Continued*).—PHYSIOLOGICAL CONSIDERATIONS.

Summary:—Contradictory Opinions of Authors with regard to the Connective Tissue of the Kidney.—Lymphatic Vessels of the Capsule and Hilum; they communicate with the Lymphatic Spaces of the Cortical Substance.—Laminar Connective Tissue in the Papillary Region.—Stellated Cells of Cortical Substance.—Connective Tissue of the Glomeruli; its Importance from a Pathological Point of View.—Brief Description of the Vessels of the Kidney.—Some Remarks upon the Urinary Secretion.—Ludwig's Theory; Bowman's.—Researches of Heidenhain.

GENTLEMEN:

We finished, at our last lecture, the subject of the normal anatomy of the *tubuli uriniferi;* we have now to consider the other elements that enter into the constitution of the kidney, namely, the blood-vessels, lymphatics, and connective tissue. Especially does the last of these merit our attention, for if a large number of renal alterations affect primarily the structure of the uriniferous canals, there are others, of no less importance, whose point of departure appears to be in the connective tissue which binds together the various elements of the organ.

I.

The existence of a connective tissue in certain parts of the kidney—the medullary substance, for instance—has never been doubted; with the cortical substance, however, it is different.

Goodsir had advanced the idea (1842) that the elements of the cortical substance were united by connective tissue. This idea was, however, combated by von Wittich, according to which observer the interstices of the secreting and excreting parts are separated from each other only by capillary vessels, without the interposition of connective tissue.

This contradiction was echoed amongst the German histologists, and the opinion of von Wittich was generally admitted, when, in 1859, Mr. Arnold Beer published a work entitled, "*The Connective Substance of the Human Kidney in its Physiological and Pathological State.*"[1] From that time the connective tissue of the kidney found itself rehabilitated; but its characteristics have been brought to light only by very recent works, and it may be said that even to-day all the questions relative to this subject are not perfectly elucidated. For the rest, there exists here, as everywhere else between the connective elements and lymphatic canals, a connection of such a character that the description of the former and the latter cannot be separated, and may be given at the same time.

A. The lymphatics of the kidneys have been of late carefully studied by Ludwig and Zawarykin. Well-formed lymphatic vessels, furnished with their own walls, and often with valves, are met with, 1st, upon the capsule of the kidney; 2d, upon the arterial and venous vessels that form the hilum.

Those of the capsule are in communication with a lacunar net-work, which occupies the thickness of the capsule. This net-work, in turn, communicates with spaces situated in the cortical substance of the kidney, between the convoluted tubes and the blood-vessels. Thus, according to Ludwig, from whom most of these details are borrowed, the *canaliculi contorti* are never in absolute contact either with each other or with the blood-vessels; these parts are constantly sepa-

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[1] Arnold Beer: *Die Bindesubstanz der menschlichen Nieren, im gesunden und krankhaften Zustande.* Berlin, 1859.

rated by fissures in which a certain quantity of liquid is always found, whose constitution does not differ markedly from that of lymph. In the pyramidal prolongations, however, the lymphatic spaces are fewer in number, while in the medullary substance they are still more rare, where they are found only in the neighborhood of the straight vessels. The lymphatic spaces of the cortical substance of the kidney are in easy communication with the lymphatic vessels of the capsules, as well as with those of the hilum; this is demonstrated by injections into the capsular lymphatics. How this communication is made anatomically, we do not know; we know only that it exists.[1]

B. The *connective tissue* of the kidney, considered by itself, has been studied particularly by Ludwig, Koelliker, and Schweigger-Seidel. According to these observers, fibrillar laminated tissue exists in the papillary portion of the medullary substance, but in the cortical substance traces are found only here and there, beneath the capsule of the kidney and about the capsules of Bowman.

In the papillary region the fibrillæ are arranged concentrically about collecting tubes, which have at this point no wall of their own. In proportion as the distance from the apex of the pyramids increases, the fibrils become more rare. In the cortical substance the connective tissue is represented only by cells situated in the intervals of the convoluted tubes and vessels. According to Schweigger-Seidel, they are stellated or fusiform cells, whose filamentary prolongations attach themselves to the walls of these canals.[2]

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[1] In fact, when a ureter is tied so as to produce in the kidney retention of the urine, a renal œdema results; the extravasated liquid occupies the lymphatic spaces, and thence easily passes into the lymphatic vessels of the capsule, and into those of the hilum. On the other hand, when in the living subject a colored liquid, as a solution of indigo, is injected into the lymphatic spaces, the urine very rapidly becomes blue. Still, we cannot, in the present state of our knowledge, admit that between the lymphatic spaces and the cavity of the uriniferous tubes there are ways of direct communication.

[2] Schweigger-Seidel, *loc. cit.*, Pl. III., fig. B, *r*.

Koelliker compares this tissue to that of the neuroglia, which forms, according to him, a genuine reticulum, a network of cells. He hesitates, however, to affirm that the prolongations in question form one body with the cells, and are not independent fibrils or fascicles. It is always the case, according to the remark of Schweigger-Seidel, that the stellated or fusiform cells have their large diameter perpendicular to the direction of the convoluted tubes.

The connective tissue of the *glomerulus* merits special mention. The capillary vessels and lobules whose *ensemble* constitutes the glomerulus are joined together by a connective stroma, which has been carefully studied by Mr. Axel Key. Between the capillaries and lobules of the cells are found stellated cells similar to those described by Schweigger-Seidel in the spaces which separate the uriniferous canals. The glomerulus is covered, besides, according to the descriptions of Koelliker and certain other authors, by a cuboid epithelium, clearly distinct from that lining the capsule, though doubtless continuous with it.

According to Virchow, Beer, and particularly Klebs, the connective tissue of the glomerulus plays a very important *rôle* in certain pathological conditions. Thus, in scarlatina, in the case of patients who have succumbed rapidly, owing to anuria, Mr. Klebs found the only lesion in the kidneys, aside from the unimportant lesions arising from congestion, to be an alteration limited to the glomeruli, and which he proposes to designate by the name of *glomerulo-nephritis*.[1] The glomeruli in these cases had the appearance of being exsanguinated, and upon a microscopical examination, either after sections were made or after dilaceration, it was seen that the number of nuclei of conjunctive cells in the meshes of the capillaries had greatly increased in number.

This excessive multiplication of the connective elements

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[1] Klebs: *Handbuch der patholog. Anatomie.* Bd. I., 2 Abth. Berlin, 1876. p. 646.

would naturally result in producing a compression of the blood-vessels of the glomeruli, which would therefore become exsanguinated. It is thus easily understood that the urinary secretion would be sometimes rapidly suppressed.

This alteration of the glomeruli, which, according to Klebs, is peculiar to scarlatina, is found in certain chronic lesions of the kidney, combined with alterations affecting the epithelium of the convoluted tubes and the interstitial connective tissue.

II.

I cannot conclude these preliminaries of normal anatomy without saying a few words about the principal arrangements presented in their distribution by the renal arteries and veins, following in this *exposé* the description given by Ludwig in his remarkable article in Stricker's Encyclopedia. It is the most recent, and, in many respects, the most fully authorized description.

The renal arteries, in their course between the medullary and the cortical substance, give origin to two orders of vessels, one destined to the cortical, the other to the medullary substance.

1. The arteries of the *cortical substance* arise perpendicularly to the direction of the renal arteries, and form the *interlobular branches;* from these spring, also at a right angle, the arterioles which run to the glomeruli, and are known as afferent vessels (*Fig.* 8). The *vas afferens*, ordinarily undivided before it reaches the glomerulus, gives off sometimes, however, branches which go directly to the capillaries. Within the glomerulus the *vas efferens* divides into four or five branches, which furnish capillaries; these then reunite to form the *vas efferens*, which emerges, at the same time as the

afferent vessel, from the side of the capsule opposite the orifice of the uriniferous tube.

The efferent vessel, after leaving the glomerulus, is directed particularly towards the medullary rays, and, at certain points where these rays are wanting, towards the most superficial convoluted tubes of the cortical layer. In the medullary rays it forms a capillary net-work with large meshes, and another net-work with elongated meshes, surrounding the convoluted tubes.

At various intervals veins are formed in these net-works, and conduct the blood into the *interlobular veins*, which, parallel with the arteries of the same name, empty into the renal veins.

2. The arteries of the *medullary substance* arise from the *vasa recta*, of which there are two kinds; those arising from the renal artery itself being, as the works of Virchow and Ludwig have shown after long disputes, real arteries. The others (which, according to Ludwig, have no muscular tunic) are *vasa aberrantia*, being vessels which are greatly elongated, arising from those of the glomeruli which are situated lowest down in the cortical substance—that is, near the medullary substance. These vessels, varying in their origin, give rise to a reticulum of capillaries more or less large, which, at the borders of the zone of limitation, communicate besides with the capillary system of the cortical layer.

Thus, in the opinion of Ludwig, which is confirmatory of that of Virchow, the circulation of the medullary substance is in part, to a certain point, independent of that of the cortical substance. This view is contrary to that of Koelliker, who pretends that, on the contrary, all the *vasa recta* spring from the afferent vessels, and that the blood circulating in them has, consequently, already traversed the glomerulus.

3. There exist in addition, in the kidney, *capsular* arteries, arising from those of the interlobular arteries that are not resolved into vasa afferentia; and, finally, arteries of *extra-renal* origin (phrenic, lumbar, etc.).

III.

It is not necessary to say more about the normal anatomy of the kidney. At present, before entering positively the domain of pathological anatomy, I deem it necessary to call your attention to some physiological facts, which will be of use at a later period.

The products of the urine known as specific, such as uric acid and urea, pre-exist in the blood. This fact has long been known, and, contrary to the recent assertions of Hoppe-Seyler and Zalesky, has been emphatically established anew. The urinary secretion is, then, a phenomenon of filtration, or rather of diffusion ; it is a special diffusion, in which the product, by reason of particular properties of the membrane, is profoundly modified.

It is of interest to us to endeavor to determine exactly in what part of the renal apparatus this selection takes place. Leaving aside the collecting tubes, which are classed by common consent as a part of the excretory apparatus, we have to consider only the secreting parts, which are composed of two principal elements : 1st, the glomeruli ; 2d, the convoluted canals and the loop system. According to Ludwig, the glomerulus is the most important part ; all the urine is there secreted with the essential principles, but in a greatly diluted state. The functions of the other parts of the kidney consist only in bringing about a progressive concentration of these principles. In the opinion of Bowman, on the contrary, adopted with some modifications by Wittich, the glomeruli serve only to separate the water, the secretion of the specific principles taking place in the special cells of the uriniferous canals.

We must recognize the fact that up to the present time

these diverse opinions are supported more by arguments than facts; the recent experiments of Heidenhain,[1] however, seem to add strength to the opinions of Bowman.

The living kidney has a special affinity for indigo; if a solution of sulphate of indigo-sodique, but slightly concentrated, be injected into the blood of an animal, a blue color, more or less pronounced, will quickly be communicated to both the urine and kidney, while a like discoloration will be given to no other part of the organism. It is the kidney, then, that in this case has concentrated the coloring matter which has been eliminated by the urine. Observe, therefore, the close analogy which exists between the results in the experiments with indigo, and what occurs in the physiological conditions in respect to urea or uric acid, specific principles of the urine.

This analogy is the conducting thread which has guided Mr. Heidenhain in his researches. In the *secretion* of the blue of the indigo, it is not alone the urine which is colored; the different parts of the kidneys are also colored in various degrees, and the knowledge of this fact, skilfully applied, should lead to interesting results. Indeed, we are justified in hoping that, by varying the conditions of the experiment, we shall succeed in determining the precise point where, in the kidney, the infiltration of the coloring matter takes place primarily, and, in a more general way, the secretion of the specific principles. If, on the other hand, it be true, as Mr. Ludwig asserts, that the secretion of the different elements of the urine (water and specific principles) takes place at the same time, and at the same point of the apparatus of the uriniferous tubes, suppression of the secretion of the water would necessarily involve the suppression of the elimination of the specific principles. The experiments of Heidenhain, however, so far as the indigo-blue is concerned, demonstrate

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[1] Heidenhain: *Versüche über den Vorgang der Harnabsonderung.* In *Pflüger's Archiv.* 9 Bd., p. 1. 1874.

just the contrary, inasmuch as the secretion of the water can be suppressed without affecting that of the coloring matter. There are two methods of suppressing thus the aqueous portions of the urine ; one of these consists in diminishing the arterial pressure in the kidney, either by an abundant bloodletting, or by section of the spinal cord below the medulla oblongata.

If, in an animal whose spinal cord has been divided, an injection of indigo be made, the following is observed : there does not reach the bladder the most minute quantity of urine, but the coloring matter passes into the kidney ; it is, then, secreted, if not excreted. In such a case, however, it is not diffused, as in a normal condition, throughout all parts of the kidney ; it occupies only a portion of the organ—the cortical substance. A careful microscopic analysis enables us, thanks to the blue tint, to determine what parts of the uriniferous tubes, and in those tubes what elements, are concerned in this elimination. The parts which are colored, then, are : 1st, the convoluted tubes ; 2d, the ascending branches of Henle's loop ; the capsules of Bowman, on the contrary, as well as the descending tubes of the loop, do not present the slightest trace of blue.

The *canaliculi contorti* and the ascending branches of the loop have, then, been shown to be possessed of independent functions. Well, these parts are the very ones that are lined with a cloudy, rod-like epithelium—that is, they are those which, by the morphological characters of their epithelium, recall the arrangement of the secreting organs.

Our investigation may be carried still farther, for the purpose of ascertaining in what elements the elimination of the coloring matter takes place. If the animal be killed ten minutes after the injection, we perceive that the coloring matter impregnates solely the epithelial cells, and in these, to the exclusion of the protoplasm, the nuclei, and the rods ; the cavity of the tubes is not at all colored. The epithelial cells are then the primary seat of the secretion, or, if you

prefer it, of the elimination of the indigo-blue. If the animal be killed, on the contrary, an hour or later after the injection, we find the epithelial cells colorless, and the blue matter to have passed into the lumen of the canals, where, owing to the absence of water, it is found in a highly concentrated state—that is, in the form of a crystalline deposit.

There is every reason for believing that phenomena essentially the same occur when the secretion of the water is allowed to continue; only, under the influence of this secretion, the coloring matter is carried away far from the primitive seat of elimination—that is, it is diffused into the descending or slender branches, into the collecting tubes, and finally into the urine. It is this that happens when, at a certain moment following close upon the injection, all the parts of the kidney, with the exception of the glomeruli, are found to be colored; but this coloration rapidly disappears when the animal is permitted to live, all the coloring matter carried by the water passing into the urine.

The other experiments of Mr. Heidenhain are, so to speak, only variations of the preceding.

The influence of the blood-pressure can be counterbalanced, even to the point of annihilating it, by augmenting, in a contrary direction, the pressure which is made in the tubes; to accomplish this result it is sufficient to ligate the ureter. At the end of twenty-four hours the secretion of urine is completely suppressed; if the solution of indigo be then injected, the result is precisely the same as in the preceding case; that is, the coloration exists only in the cortical substance, in the rod-like epithelium.

Finally, there is an elegant variation in the experiments of Mr. Heidenhain: the surface of the kidney in a living animal is cauterized lightly with the nitrate of silver, so as to form transverse bands, two or three days after which an injection of indigo is made. This cauterization, by a mechanism not yet made clear, has the effect of suppressing, in the corresponding parts of the kidney, the secretion of water. Now,

while in the zones corresponding to the portions not cauterized the coloration affects the cortical and medullary substance, we perceive, on the contrary, in the zones which correspond to the cauterized parts, that the cortical substance alone is colored. A microscopic examination shows, besides, in this case, as in the preceding experiments, that the coloring matter impregnates the convoluted tubes and the ascending branches of the loop, to the exclusion of the glomeruli and all the other parts of the apparatus.

As a *résumé*, these experiments tend to demonstrate : 1st, that the secretion or elimination of the coloring matter is independent of the secretion of the watery portion of the urine, or, at all events, that the coloring matter carries with it only the small quantity of water necessary to hold it in solution in its passage through the walls of the tubes ; 2d, that this secretion takes place in special points of the apparatus—those which are covered by a cloudy epithelium ; the glomeruli do not appear to enact any part therein, and seem to have no other *rôle* than to furnish the aqueous part of the urine.

Does the secretion of the specific principles of the urine take place in precisely the same fashion as the elimination of coloring matters ? As regards urea, it is probable that it does, but it cannot be demonstrated experimentally, since urea produces no coloration upon the parts where it is eliminated, and does not become concrete in the midst of the liquids of the organism. It is not the same, however, with *uric acid*, or, still better, *urate of soda ;* in fact, in the experiments of Mr. Heidenhain, the urate of soda injected in a concentrated solution is deposited in the *canaliculi contorti*, in the form of yellow granulations accumulated in the lumen of these tubes, while there is not found in the glomeruli the slightest trace of it. In the experiments in which the secretion of water has not been completely interrupted these granulations are found to extend to the collecting tubes ; it is, however, easy to recognize that in these, the deposits of urates

come from the portions higher up, as they are more voluminous than those found in the convoluted tubes, and present concentric layers, which have become stratified as they have advanced in their journey through the uriniferous tubes, at the same time as the secreted urine has undergone a progressive concentration.

The result of these injections of the urate of soda recall what is observed, in a normal condition, in birds, whose solid urine is, you know, composed, to a great extent, of glomeruli of uric acid. According to the observations of von Wittich, these glomeruli already exist in the rudimentary state in the kidneys of the bird as far as the tubuli contorti, and even in the epithelial cells of these tubes, where they occupy the nucleus, but are never met with in the capsules of Bowman. In the other parts of the uriniferous tubes there are found free cells, in which the glomeruli acquire dimensions more and more considerable.

We may now, gentlemen, bring to an end the long anatomical and physiological excursion upon which I have conducted you. We shall have, I hope, no cause to regret the time we have given to it, for, on more than one occasion, the facts we have collected in our journey will be usefully applied to the interpretation of phenomena belonging to the domain of pathological anatomy, a domain which we may now enter with unembarrassed footsteps.

LECTURE III.

TUBULAR INFARCTUS OF THE KIDNEY—URINARY CASTS —SUMMARY OF VIEWS OF BRIGHT'S DISEASE.

Summary:—Crystalline Tubular Infarctus of the Urate of Soda.—Masses of Uric Acid (Gravel of the Kidney).—Uratic Infarctus of the New-Born; Opinions of Virchow and Parrot.—Calcareous Infarctus.—Renal Tubulhæma.—Biliary Infarctus.

Fibrinous or Urinary Cylinders or Casts.—Undue Importance Attached to the Presence of these Cylinders in the Urine.—Study of these Cylinders in the Kidney by the Aid of Anatomical Processes.—Seat of the Cylinders.—Circumstances under which they are met with: in the Region of the Straight Tubes; in the Convoluted Tubes.

Study of Urinary Cylinders or Casts in the Urine.—Varieties in Form and Size.—Varieties in Respect to Optical and Micro-Chemical Characteristics.—Hyalin Casts: Granular; Waxy; Epithelial.

Clinical Signification of Urinary Casts.

View of the Ensemble of Bright's Disease.—Doctrines of the Unicity and Multiplicity of Forms.—General Characters of the Different Forms: the Large White Kidney; the Contracted Kidney; the Amyloid Kidney.

GENTLEMEN:

I will first call your attention to a group of renal alterations to which, perhaps, is not generally accorded as much importance as they seem to me to merit, both from a theoretical and practical point of view. I refer to *tubular infarctions of the kidney*. The various uriniferous canals may be, indeed, more or less completely obliterated by products secreted with the urine, or which are mingled with this liquid in its course.

1. I will mention first the *crystalline infarctions of the urates* resulting from the obliteration of the uriniferous tubes by the white crystalline urate of soda, and which is observed frequently in gouty subjects at the same time, as one of the

forms of chronic interstitial nephritis. These deposits, which are visible to the naked eye, are seen in fine striæ, of a chalky whiteness, in the tubular substance, and are situated principally in the papillary region; they have never been found elsewhere than in the collecting tubes. I have been able to show, in researches previously made in conjunction with M. Cornil,[1] that these deposits are composed of two parts: one central, amorphous, occupying the canal whose lumen it obstructs; the other, crystalline, is found in the form of long needles, which extend in every direction in the intervals of the tubes. These uratic infarctions thus obliterate a certain number of papillary orifices, and although they are seldom very numerous, it does not seem impossible that when they occupy a considerable portion of the papillæ of both kidneys they should contribute to the production of the grave symptoms of gouty anuria or ischuria.

2. Next to crystalline uratic infarctions must be mentioned a form of gravel that may be called *gravel of the kidney*, and which has also been found by Rayer to exist in gouty subjects. I refer to uric acid of a yellow tint, and which is found in the form of small amorphous masses occurring at the same time in the cortical layer and pyramids; a large number of small grains of the same character are met with in the pelvic cavity.

3. There is still another form of the *uratic infarctus*, which has been made to play an important rôle in the pathology, or rather the physiology of the new-born. It consists of small blackish masses, already described by Rayer, but which have been more successfully studied by Virchow and Mr. Parrot. Formed by concretions of urate of ammonia (Virchow) or urate of soda (Parrot) accumulated in the collecting tubes, they present themselves in the shape of tufts on the cut surface of the pyramids.

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[1] *Mém. de la Soc. de Biologie*, 1863, Pl. IV., Fig. 3, et *Leçons sur les maladies des vieillards*, Pl. III., Fig. 3.

According to Virchow, these are found in more than half the cases in new-born children, but only from the second to the nineteenth day; he considers their formation a physiological fact, occurring only in infants that have breathed, and he proposes to derive from their presence a fact of importance in legal medicine. Parrot regards it, however, as a pathological fact, occurring only as a result of grave intestinal troubles, when there is a deficiency of the aqueous element in the organism; Mr. Parrot has likewise met with it at a period much more remote from birth than that mentioned by Virchow, as, for example, in infants five, six, and even nine months old.

4. I will simply mention the *calcareous infarctions* which we may meet with in old people, and which, according to Koster (cited in Henle), occupy Henle's loops.

5. Mr. Parrot has recently described, under the title of *tubulhæma*, sanguine infarctions of the canals produced sometimes in the new-born; the pelves in these cases contain a blackish magma resembling pitch. The collecting tubes at the same time are obliterated in large numbers, by cylindrical masses formed by blood-cells agglomerated, and more or less profoundly altered, but still easy of recognition. The masses composing these cylinders are met with isolated, and of moderate size, in the convoluted tubes and in Henle's loop. It is probable that a transudation of blood-cells, rendered possible by the alteration of the blood, takes place. There is always a possibility, as a result of the obliteration of a certain number of tubes by the infarctions from concrete blood, of the development of uræmic accidents capable of rapidly producing death.

6. In icterus, where the discoloration is very deep, the bilirubin may become concentrated in the urinary liquid, forming *biliary infarctions*, which obstruct the straight tubes, as is shown in a plate of Frerichs' atlas (Taf. I., fig. 9). I am not aware that any accidents have ever been found to result from the presence of these biliary concretions of the kidneys.

7. Of all the tubular infarctions, the most interesting to study are incontestably those designated as *fibrinous casts*, but which I should rather call *urinary casts*, inasmuch as they are not composed of fibrin.[1]

II.

You are aware, gentlemen, how much importance clinical observers generally attach to the investigation of these casts in the urine; as they come from the depths of these tubes, whose internal moulds they represent, it is supposed that information may be derived from them in regard to the anatomical condition of these tubes. This view is an ingenious one, but its practical application, I believe, has been singularly exaggerated.

The urinary casts are to be studied in two ways: *A.* In the kidney itself, by the aid of anatomical processes; *B.* During life, in the urine.

A. A study of the casts in the urine enables us to recognize the locality in which they are formed. The capsules of Bowman have never been found to be obstructed by the matter of which they are composed; but, except in this point, they may be met with nearly everywhere in the uriniferous canals. It is, however, most of all in Henle's loop, particularly in the ascending branch, that they are met with in the greatest abundance; they are also frequently met with, of various diameters, in the collecting tubes. At these two points they are easily recognized upon longitudinal or transverse sections, and it can be shown that epithelial cells do

[1] Consult upon *casts* an interesting work by Dr. A. Burkart: *Die Harncylinder mit besonderer Berücksichtigung ihrer diagnostischen Bedeutung.* Berlin, 1874.

not ordinarily enter into their constitution. They are found in the centre of the tube, in the form of a transparent, amorphous mass, sometimes granular, or, rather, containing in its interior variously shaped bodies, leucocytes, blood-globules, *débris* of cells, etc. When they have been retained a long time in the kidney, as, for example, in chronic lesions of this organ, they usually present a yellowish tint, and are easily colored either by iodine or carmine.

Urinary casts may be found, under certain circumstances, in the *region of the straight tubes:* 1st. In the normal condition, according to Klebs and Axel Key. 2d. In animals covered experimentally with varnish, and thus rendered albuminuric. Krause (cited by Henle) has found casts in Henle's loops. 3d. They are found, above all, in various forms of Bright's disease. 4th. In steatosis resulting from phosphorus-poisoning; according to the observations of Mr. Ranvier, they are found in small numbers in the straight tubes, but mostly in Henle's loops. In the last case epithelial cells enter into the constitution of the casts, which are presented in the form of a fatty granular magma, composed of an albuminous mass and of fatty granulations.

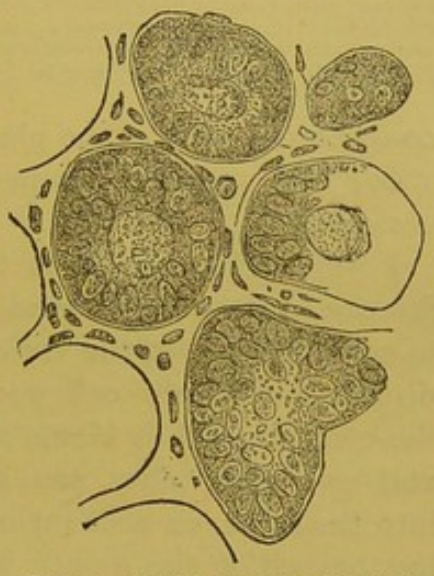

FIG. 10.—*Section through a kidney affected with Bright's disease.* The cells which line the tubes are granular, filled with proteiform and fatty granulations. In the centre of the tube is seen the *section of the hyaline casts.* Magnified 420 diameters. (Cornil and Ranvier.)

Casts more or less analogous to the preceding may also be formed, under certain conditions, in the *convoluted tubes;* thus, in parenchymatous nephritis, the lumen of these tubes may be found obstructed by a mass, hyaline in the centre and granular at the periphery; this appearance is produced by a cast surrounded by altered epithelial cells. In advanced interstitial nephritis, where, in consequence of the

disappearance of the epithelium, the uriniferous tube is represented only by the basement membrane, the canal is completely filled by a colloid substance, in which the cast is found

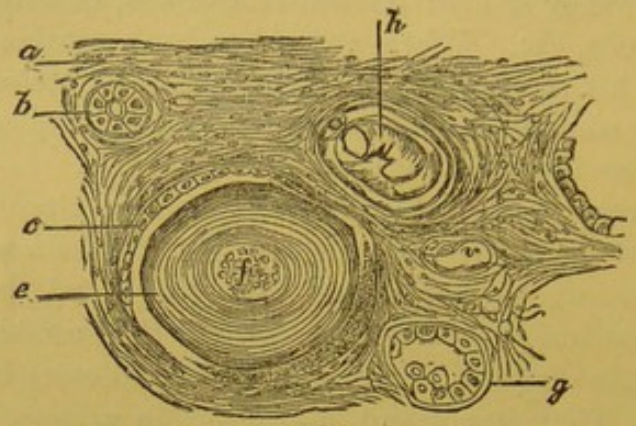

FIG. 11.—*Section of kidney in a very advanced stage of interstitial nephritis.*—*a*, Connective tissue formed by fibres and flat cells.—*b*, Section of an atrophied uriniferous tube, presenting in the middle of its lumen the section of a small colloid cast.—*h*, A uriniferous tube also containing a colloid cast, the epithelial cells of which are flattened.—*g*, Uriniferous tube.—*c*, Flat cells of the covering of a cyst formed at the expense of the uriniferous tubes, and containing a colloid substance, *e*, with concentric lamina, and a granular central mass, *f*, formed of granulations of hematine.—*v*, Blood-vessel. Magnified 200 diameters. (Cornil and Ranvier.)

comprised. Two of the plates of Mr. Cornil (Thèse d'agrég., 1869) will accurately represent to you these two different varieties.

I will confine myself to the above examples, since the infarctions of the convoluted tubes are to be studied especially in connection with the various anatomical forms of Bright's disease, but would call your attention to the fact that only the casts formed in Henle's loop, or in the junctional canals and collecting tubes, can, according to all appearances, pass into the urine, on account of the small calibre of the descending branch of the loop. The casts of the convoluted tubes can, indeed, pass through this narrow branch only with the greatest difficulty, and we cannot expect to find them often in the urine. This fact is a very important one, and detracts greatly from the value of the clinical investigations of casts, since the very ones whose existence it would be of the most importance to discover seldom find their way into the urine.

We should now, gentlemen, study the urinary casts as they

are found during life in the urine; on examining the collections which are formed in this liquid after reposing, by the microscope, several varieties are easily recognized.

a. The *volume* and *form* of the urinary casts are most liable to vary according to the locality in which they are formed. The largest are supposed to originate in the collecting tubes; those of medium size, in collecting tubes of small calibre, or in the intermediate piece; the smallest doubtless come from the ascending branch of Henle's loop. Klebs and Dickinson have described cylinders of considerable size, and with a tapering extremity; this slender end probably corresponds to the ascending branch, or to the intermediate piece. Mr. Cornil has represented in his thesis on aggregation (p. 24, Figs. 5, 5°) a cast presenting a constriction and two enlarged portions; the narrow part doubtless corresponds to the intermediate canal or junctional canal of Schweigger-Seidel.

b. In consequence of certain varieties in the *optical* or *micro-chemical* characteristics of the urinary casts, several groups of them may be established:

1. The hyaline casts are formed of an amorphous substance, not colored, slightly refractive, flexible, and not friable. Rovida, who has analyzed them (*Centralblatt*, 1872), found them to be composed of an albuminous substance, differing from chondrine and fibrine, and bearing most resemblance to gelatine. As long ago as 1855, Mr. Robin had protested against the name of "*fibrinous*" *casts*, employed even now sometimes, and which is founded only upon coarse analogies. Upon the surface or in the interior of these hyaline casts may be found leucocytes, blood-globules, cell-nuclei, or even epithelial cells, more or less loaded with fatty granulations.

These are the most common of all the urinary casts; they are met with in renal affections the most diverse, acute or chronic, and may even be found in a normal state, and in conditions where the structure of the kidney is unaltered.

2. There are two varieties of the granular casts. The

first have the same origin as the preceding, but have undergone a sort of *granular degeneration*. They become transparent under the influence of acetic acid (Dickinson). The presence of these casts, recognized for a long time in the urine, is, according to Mr. Dickinson, of considerable significance, as denoting a lesion of the kidney essentially chronic, particularly interstitial nephritis. From these granular casts must be distinguished the *fatty granular casts* described by Ranvier in steatosis, the result of phosphorus-poisoning. Found in acute conditions, the existence of these last should awaken attention to the possibility of poisoning by phosphorus.

3. The *waxy casts* resemble in many respects the hyaline, but possess greater refractive powers, and have generally a

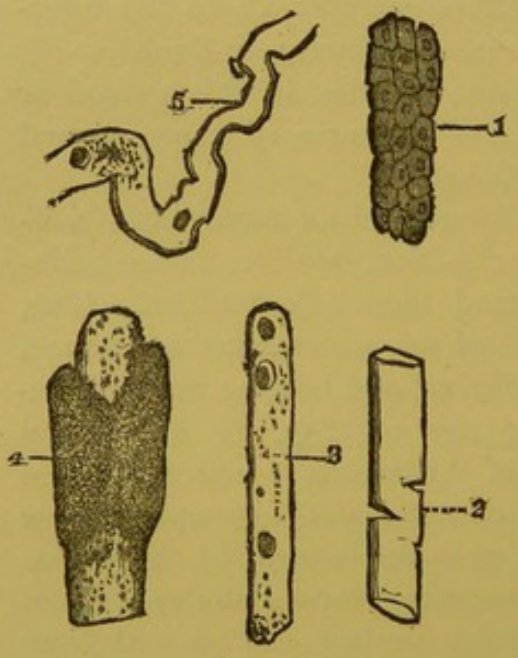

FIG. 12.

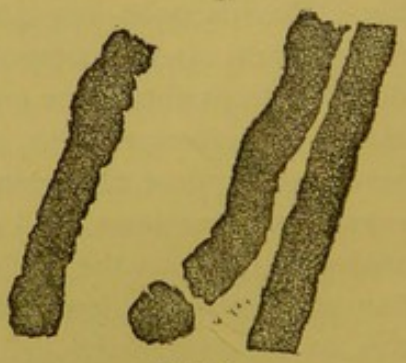

FIG. 13.

FIG. 12.—*Hyaline casts in albuminous nephritis.*—1, Cells of the kidney.—2, Hyaline cast with broken edges.—3, Cast with fragments of cells adhering to its surface.—4, Hyaline cast covered with fatty granulations.—5, Convoluted cast. (Cornil and Ranvier.)

FIG. 13.—*Full, fatty, albuminous casts in albuminous urine, in poisoning by phosphorus.* (Cornil and Ranvier.)

yellowish coloration; they are also more friable, and their borders are, as it were, notched. They offer more resistance

to reagents than do the hyaline casts, but color easily upon the action of coloring matters, particularly carmine, and more especially iodine, which communicates a brownish yellow tinge. The waxy casts are met with most often in interstitial nephritis ; they have no particular connection with amyloid degeneration of the kidney.

4. We must not confound with urinary casts bodies of renal origin correctly designated as *epithelial casts*, which are really conglomerations, sometimes exclusively composed of epithelial cells massed together, more or less altered, and originating in the uriniferous tubes. In certain acute maladies, as in eruptive fevers, their presence in the urine is of but little importance. They are also often found as a result of the administration of diuretics. It may be said that, from a clinical point of view, they do not possess much importance.

c. After what I have said in the course of the preceding description, there remains but little to add concerning the *clinical significance* of the various forms of urinary casts. I will limit my remarks to the following :

1. In a general way, the clinical importance of urinary casts has been greatly exaggerated. They are *not*, as they have been called, " faithful messengers announcing to the clinical observer the anatomical condition of the kidney " ; " mirrors reflecting the various renal lesions." Formed in the ultimate parts of the apparatus of the tubuli uriniferi, they can only, in any case, furnish information upon the condition of these parts. I have previously maintained the fact that the casts formed in the convoluted tubes can but very seldom pass into the urine.

2. Hyaline casts may be found in the urine in normal conditions. This fact, first pointed out by M. Robin in 1855, has been confirmed by Axel Key, Rosenstein, and many other authors.[1] They are also met with in various other

[1] Only hyaline casts, more or less pure, and not granular or waxy casts, are referred to here.

affections than those of the kidney, and even where there is no albuminuria. Thus, Nothnagel (*Deutsche Archiv*, 1873, p. 326) says that he constantly found them in cases of severe icterus, accompanied by elimination of the biliary acids by the urine, without reference to the origin of the jaundice, whether from catarrh, pneumonia, pyæmia, etc. The formation of the casts seems due in these cases to the action of the biliary acids upon the blood, for Leyden has found them in the urine of animals whose blood he had injected with biliary acids.

Even when renal disease exists, the hyaline casts are of no interest, except from their long persistence. Where they have been observed for a long time and in large numbers in the urine, they indicate, as a rule, a confirmed lesion of the kidney; I should remark here, however, that there are other and more important signs which suffice to throw light upon the true conditions which exist.

The granular casts are of the most importance, and when they are found for a certain time at each examination, in copious and moderately albuminous urine, denote, according to Mr. Dickinson, interstitial nephritis. Their presence may then aid in establishing the diagnosis of the *form*, and, even in doubtful cases, the positive diagnosis of the *disease*. The waxy casts also indicate a chronic lesion, but it should be understood that the brown tint communicated to them by the action of iodine does not necessarily indicate amyloid degeneration of the kidney.

3. Finally, the lesions of Bright's disease may exist without any casts being found in the urine; they are formed in the kidney, but retained in the pelvis. This occurred in a striking manner in a case of parenchymatous nephritis observed by M. Ackermann (*Centralblatt*, 1872, p. 606): the examination of the urine did not, at any time during a period of several months, reveal the existence of casts; but after death about eight grammes of an orange-yellow mass were found in the pelvis and calices, which a microscopic examina-

tion showed to be composed of a great number of yellow, homogeneous cylinders. This fact accounts for a circumstance already mentioned—that, in the course of Bright's disease, a temporary suspension of emission of casts sometimes occurs.

These remarks comprise what I wished to say to you concerning the semeiological value of urinary casts. I shall have occasion to revert to this subject in connection with the various forms of Bright's disease.

III.

I now propose, gentlemen, to study somewhat in detail the various alterations which are ordinarily comprised under the ordinary title of *Bright's disease.*

You are aware that, in the opinion of the greater part of French or German physicians, the various alterations of the kidney discovered in autopsies of such subjects as during life have suffered from albuminuria and anasarca, correspond to the various successive phases of the same, or to one, morbid process. This opinion represents a doctrine which may be termed the *theory of the unity* of Bright's disease.

According to another doctrine, not of the *duality*, but of the multiplicity, in the forms of Bright's disease, the various forms of renal alteration revealed by the autopsy represent, not the successive phases of the same process, but so many distinct anatomical states with which are connected during life as many well-characterized symptomatic groups. This doctrine might be called the English theory, since it is especially in England that it has for twenty years been sustained and developed.

I have been a long time a convert, gentlemen, to this doc-

trine, and this is the point of view I adopt in laying before you the anatomo-pathological history of Bright's disease or *diseases.*[1] In my opinion, therefore, which is only, so to speak, the reflex of the English theory, Bright's disease is a class comprising several distinct species, not only from an anatomo-pathological point of view, but as regards etiology and symptomatology.

I will to-day content myself with pointing out to you in a summary view the anatomical and clinical characters which distinguish these species, of which I will give you later a separate description.

All the species I shall treat of are either *snbacute processes*, or are *primarily chronic*, for I do not in the frame of the picture of Bright's disease, include the acute forms of renal affections that are ordinarily referred to this disease. Farther on Is hall justify this exclusion.

A. First Variety.

Parenchymatous Nephritis—Etiology.—The disease is met with especially in young subjects, rarely at an advanced age. Causes often unknown; markedly influenced by damp cold; sometimes preceded by scarlatina.

Evolution relatively rapid; three, six months, a year.

Symptoms.—a. Œdema, anasarca, dropsies of the parenchyma and serous cavities. *b.* Urine usually scanty, often turbid and high-colored, containing a considerable proportion of albumen; density seldom below the normal; sediment abounding in hyaline casts. *c. Ordinary complications:* purulent pneumonia; gangrene, erysipelas of the œdematous parts; uræmic symptoms less frequent than in the

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[1] The same views have been sustained in publications which have appeared since these lectures were given: Lecorché, Lancereaux, Cornil and Ranvier, Bartels, Labadie-Lagrave, etc.

second form, and often provoked by inopportune treatment (purgatives, vapor-baths).

Anatomical characteristics.—The kidney is large, heavy, its surface smooth ; upon section the cortical substance seems voluminous, its color lost, and wanting in vessels. It is the "large white kidney," the "*large smooth kidney*" of English authors, *Bright's kidney, par excellence*, very well represented in Plate II., Figs. 1, 2, and Plate IV., Figs. 1, 2, in the Reports of Medical Cases.

Histologically, the lesion affects principally the epithelium of the kidney ; the connective tissue, when altered at all, is so only secondarily.

This form, which corresponds to the *second stage* of the advocates of the theory of the unity of Bright's disease, is sometimes designated by the name of *parenchymatous nephritis*. This title is wrong, as it prejudges the nature of the process, which is far from being understood ; but as you are doubtless familiar with it, I believe I should retain it.

B. Second Form.

B. Interstitial Nephritis—Etiology.—Subjects affected by it succumb between the age of fifty and sixty ; etiological conditions but little known ; the influence of gout, lead-poisoning, and alcoholism appear, however, to be well demonstrated.

Evolution very gradual ; the disease always of a chronic character ; may last several years—ten years, for example.

Symptoms.—Œdema is absent in more than half the cases ; often it is scarcely appreciable. *a.* Urine abundant, at least in the first stage ; sometimes real polyuria ; it is clear, pale, of a feeble specific gravity ; albuminuria slightly marked, and may be absent from time to time ; the urine contains but few casts. At an advanced period, however, œdema supervenes, or augments if it previously existed, and the albumen may be found in the urine in greater quantities.

b. Complications quite frequent, constituting one of the most important characteristics of this form: hypertrophy of the left heart without valvular lesion; albuminous retinitis, almost peculiar to this form; hemorrhages from various passages; frequent arterial atheroma; visceral inflammations, pneumonia, pericarditis, etc. This class of cases generally terminates in uræmia.

Anatomical characters.—Kidney small, being only half its normal weight; the capsule is closely adherent; the surface of the kidney is of a reddish tint and has a sandy, granulated appearance; the granulations, small, nearly uniform in size, are regularly disseminated over the surface of the kidney, which presents here and there small cysts.

Section shows that the atrophy affects the cortical substance, which may be reduced to a thin layer. This is the *contracted kidney*, the *granular kidney*, the *small red kidney*, which is still called *gouty kidney*, or sometimes *saturnine kidney*.

Histologically we have to deal with a genuine cirrhosis of the kidney; the connective tissue is primarily affected, the epithelium being affected only consecutively. It is, then, an interstitial nephritis; this form of nephritis, exceptionally primitive, is the only one that is entitled to appear in the delineation of Bright's disease; calculous interstitial nephritis, which supervenes from distention of the pelvis, is to be nosographically separated from it.

C. Third Form.—*Amyloid Kidney.*

The third form has been, in all recent writings, distinctly separated from the ordinary Bright's disease. It is characterized anatomically by the alteration known by the name of *amyloid kidney*, which, while it presents the general appearances of the large white kidney, possesses special chemical characteristics. The alteration affects primarily the small vessels; the connective tissue and parenchyma are affected

only secondarily. There are generally found, at the same time with the renal alteration, similar lesions in the spleen, liver, intestines, etc.

The *etiological conditions* are very distinct: scrofula, syphilis, tuberculosis, prolonged suppurations, etc. The amyloid kidney may be met with at all ages, but oftenest between the ages of twenty and thirty.

Clinically this form resembles the preceding in the slowness of its evolution, in the infrequency of œdema, and in certain characters of the urine. Those affected often present a specially marked, cachectic taint, but the most important differential characteristics are derived from etiological circumstances, from the concomitance of other affections in the liver, the intestine (diarrhœa), etc., and, finally, from the nature of the complications; thus we seldom observe, coincident with the amyloid kidney, hemorrhages, retinal lesions, or hypertrophy of the heart; uræmia is also comparatively rare, and death supervenes generally from the existence of concomitant lesions, particularly diarrhœa.

LECTURE IV.

OF CONTRACTED KIDNEY (*Interstitial Nephritis*).

Summary:—Historic Considerations.—Lesions of the Kidney in Interstitial Nephritis at the most advanced Stage.—Granulations.—Histological Study.

Lesions of the Kidney in the First Period of Interstitial Nephritis.

Analysis of the Histological Alterations of the Kidney.—Connective Web; Uriniferous Canals; Various Kinds of Cysts; Lesions of Bowman's Capsules and of the Glomeruli; Alterations of the Arteries.

GENTLEMEN:

Before proceeding farther in the description of the various renal lesions generally connected with Bright's disease, I wish to recall to you the point of view from which I pursue the study of these lesions.

In my opinion, as I have already stated, the various forms of renal alterations in question do not represent the successive phases of one and the same morbid process; some of these alterations, at least, constitute anatomo-pathological states fundamentally distinct, to which correspond, during life, as many well-marked symptomatic groups, which enable us to mount upward from the symptom to the lesion, and to form a special diagnosis and prognosis.

I have briefly indicated the fundamental types, to the number of three, which should be made the object of a particular description. The two first types, which, to the partisans of the theory of unity, represent the second and third degrees of Bright's disease, correspond to the alterations we have designated as the *large white kidney*, *large smooth kidney*, etc. (parenchymatous nephritis), on one hand, and as the *con-*

tracted or *granular kidney*, *small red kidney*, *gouty kidney* (interstitial nephritis) on the other; the third type is represented by the amyloid form.

I.

The distinction I propose to establish does not extend very far back, for it is hardly twenty years since the doctrine of there being distinct forms of Bright's disease came into existence.

In the famous work which forms a part of the collection of medical observations relating to diseases which terminate in dropsies, Bright himself already gave this question consideration; nevertheless, he broached the subject in a hesitating manner, and, on the whole, seemed unable to arrive at any conclusion. "I have been led to believe," he says, "that the kidney in renal dropsies is affected by various forms of disease;" but elsewhere he says, "I am not certain that these views are correct," and adds that the three forms he has described are perhaps only modifications or stages more or less advanced of one and the same disease.[1]

Rayer is a little more explicit: the alterations of the kidney in albuminous nephritis may be, according to him, connected with six principal forms, "probably successive."

The majority of authors who have followed, have favored the doctrine of unity, which numbers among its adherents Frerichs and most of the physicians who, in France as well as Germany, have up to the present time written on Bright's disease.

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[1] R. Bright: *Reports of Medical Cases*, p. 67 and p. 69. London, 1827.

The first opponents to this doctrine have arisen in Bright's own country, England. Todd, Wilkes, Quain, and G. Johnson were the first to reject the generally received theory; the last is particularly positive on this point, and brings to bear in favor of the doctrine he embraces, in addition to anatomo-pathological facts, an argument derived from the domain of clinical experience, an argument to my mind very significant and which should be adduced here.

"The subjects at whose autopsy," says Johnson,[1] "the large white kidney of Bright is found, have almost without exception had some dropsical affection at some period of their clinical history; on the contrary, those who succumb from small, contracted kidney, have never suffered in the slightest degree from dropsy." And he gives statistics which show that in twenty-six cases of the large white kidney, twenty-four were affected with dropsy, while out of thirty-three cases of contracted kidney, it occurred only fourteen times, and, even in these cases, was scarcely perceptible.

These facts clearly contradict the hypothesis according to which the contracted kidney has passed by a corresponding phase to the large white kidney; for it would be incomprehensible, if there were any foundation for this hypothesis, how the majority of subjects having the contracted kidney could escape during the entire course of their long disease the dropsy, which is, so to speak, the rule in that form characterized by the large white kidney. This argument is of no little importance, but, as we shall see, is far from being the only one that can be adduced in favor of the English theory.

This doctrine counts in England among its supporters, in addition to the authors already mentioned, Mr. Goodfellow, author of an interesting work, particularly from a clinical point of view (1861); Mr. Dickinson, whose treatise on the pathology and treatment of albuminuria (1860) contains one

[1] Medico-chir. Transactions. 1859. p. 156.

of the earliest good descriptions of interstitial nephritis; and finally, Mr. Grainger Stewart, whose work, published in Edinburgh, bears the characteristic title: *Treatise on Bright's Diseases.*[1]

In Germany, Mr. Traube has endeavored for a long time to separate anatomically and clinically interstitial nephritis and the amyloid kidney from parenchymatous nephritis; it is only the first of these that, in his opinion, can be called Bright's disease. Finally, M. Bartels, in a letter published in the collection of Mr. Volkmann, announces himself as an absolute partisan of the English doctrine.

In France, this doctrine has as yet only a small number of adherents; M. Lancereaux seems inclined to connect himself with it in some passages of his *Atlas d'anatomie pathologique* (1871); the same with M. Lecorché, author of an interesting memoir entitled: *Néphrite interstitielle hyperplastique ou sclérose du rein* (Archiv. de Méd., 1874); but the most important work, in my opinion, on this subject, particularly from the anatomo-pathological point of view, is that of M. Kelsch, *Agrégé* at the Val-de-Grâce; this work, at once critical and founded upon anatomical and clinical observations made by himself, is published in the *Archives de Physiologie* (1874).[2]

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[1] T. Grainger Stewart: *A Practical Treatise on Bright's Diseases of the Kidneys.* 2d edit. Edinburgh, 1871.

[2] These lectures on Bright's disease were delivered during the summer trimestre of 1874, and published shortly after in the *Progrès Médical.* Since this date several contributions have appeared on the same subject; I will mention only the following:—Lecorché: *Traité des Maladies du Rein.*—Lancereaux: article *Rein* of the *Dictionnaire Encyclopédique des Sciences Médicales.* 1875.—Bartels: *Handbuch der Krankheiten des Harnapparatus,* in Ziemssen's Handbuch. 1875.—Edward Bull: *Klinische Studien über chronische Bright'sche Krankheit.* Christiania, 1875; analyzed in *Virchow's Archiv,* 67 Bd., 2 Heft, 1876. See also an interesting article of M. Labadie-Lagrave, in the *Revue des Sciences Médicales,* 4th year, Vol. VIII., 2d fascicule, p. 768, 1876.—All these concur in the multiplicity of the forms of Bright's disease.

II.

I hasten now, gentlemen, to reach the descriptive part of my subject, and will commence by the *exposé* of the alterations peculiar to the *contracted kidney*, or, if you prefer it, *primitive chronic interstitial nephritis*. I will suppose, to begin with, a case in which the alterations are presented in their condition of perfect development—for example, a case of a gouty subject, who has voided for years albumen in the urine, without œdema ever existing, and who has succumbed from the accidents produced by uræmia.

The autopsy shows that the kidneys are small, and about equally contracted (Plate I.); their weight is about that of the normal. They present a firm consistence and a general red color; but upon removal of the capsule, which is thick and adherent to the subjacent parts, there are seen to be scattered here and there upon the surface, small elevations nearly uniform in size and of a gray or yellow color, offering in this respect a marked contrast to the neighboring parts, the color of which is red, more or less bright in hue. Sections show that the atrophy affects principally the cortical substance, the medullary being much less affected. As a result of the diminution in the size of the kidney, the pelvis has the appearance of being more or less considerably dilated.

Let us now ascertain to what histological alterations these appearances correspond, for which purpose we will first examine, by the aid of a feeble magnifying power, sections of the kidney prepared by the aid of the picro-carminate of ammonia, a reagent which, as you are aware, possesses the property of coloring more vividly elements of recent formation.

If the section be made parallel to the surface of the kid-

ney, and not far from this surface, it will necessarily include a certain number of neighboring lobules. This, then, is what we discover in examining the various regions that compose these lobules, the normal disposition of which it is scarcely necessary to recall to you.

1st. In the centre of the lobule are found the collecting tubes, whose epithelium presents various degrees of fatty-granular degeneration, and whose lumen is obstructed by hyaline or waxy casts. 2d. About this central region we search in vain for the convoluted tubes ; these seem to be replaced by a zone of a red tint, produced by the carmine. A careful examination soon shows that this coloration is due to the presence of a considerable number of young elements, round or fusiform embryonic cells. With a little attention

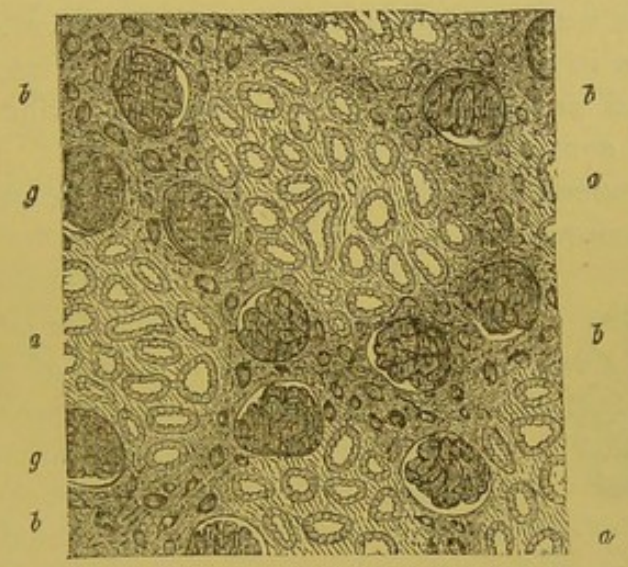

FIG. 14.—*Section of contracted kidney, made perpendicularly to the direction of the lobules.*—The clear portions, *a*, form the granulation, and correspond to the centre of the lobule ; they represent the section of the collecting tubes.—The dark portions, *b*, which circumscribe the granulation, are formed by the convoluted tubes, atrophied by the embryonic tissue of new formation, and by the glomeruli, *g*. (Half diagrammatic figure, after preparations of M. Kelsch.)

we discover in this red zone the lumen, singularly contracted and comparable to a thread, of the convoluted tubes, which at first remained unperceived. Some of them still contain traces of glandular epithelium in process of granular-fatty

degeneration ; the greater part are deprived of this epithelium, and are carpeted frequently with a row of young cells, which form a new epithelial covering, entirely different from the old one ; finally, many of the tubes are filled with granular or transparent casts. 3d. Outside of this zone are seen the Malpighian bodies, enveloped in a thick capsule composed of several layers. The glomerulus itself has undergone various alterations, which will be considered hereafter.

I have now placed before you, gentlemen, the elements necessary to the recognition of the topographical disposition of the lesions which exist in interstitial nephritis, and also to the comprehension of the reason of the existence of the granulations.

In fact, the alteration specially affects, you perceive, the connective web enveloping the convoluted tubes. This web undergoes in the beginning a transformation into embryonic tissue, and becomes replaced at a later period by a well-organized connective stroma.

This connective new-formation has had the effect, doubtless by compression, of producing atrophy of the convoluted tubes whose epithelium has suffered, become disintegrated, and at a later period has become replaced by a lining of young cells ; finally, the parts which compose the region of the labyrinth have become atrophied and collapsed. The central part of the lobule, on the contrary, has remained, relatively, but little altered, and the collecting tubes which compose it mainly, remain with nearly their normal dimensions. You will easily understand that the salient *granulations* upon the surface of the kidney correspond to this central part of the lobule ; they present a color sometimes gray, sometimes red, according as the epithelium of the collecting tubes has become fatty, or,

FIG. 15.—*Uriniferous tubes, atrophied, and containing small cells, partly disintegrated, and fatty granulations.* —Magnitude of 420 diameters. — Compare the diameter of these atrophied tubes with those of Fig. 332, drawn after being equally magnified. (Cornil and Ranvier.)

on the contrary, has remained normal. The small red collar which surrounds the base of each granulation corresponds to the highly vascularized, but atrophied region of the labyrinth.

If the section be made perpendicularly to the surface of the kidney, we discover still, as in the preceding case, that the medullary rays in the cortical region are but slightly altered; only the collecting tubes become somewhat tortuous. Outside of the medullary rays, in the region of the labyrinth, the convoluted canals are represented, as was just stated, by very narrow tubes, sometimes being dilated here and there, and separated from each other by embryonic or more or less organized tissue. The Malpighian bodies which mark the limits of the lobules have, on account of the atrophy undergone by the convoluted tubes, the appearance of being brought much nearer to each other than in a normal state.

Such is the constitution of the granulation, well comprehended in M. Kelsch's work, being very easy to confirm by the preparations of that anatomist which I hold in my hands, and which, besides, have been pointed out by Mr. Wilks. The granulations of the contracted kidney must not, however, be confounded with the spots which are found upon the large white kidney, either on the surface or upon making sections in the cortical substance, the constitution of which is quite different. These latter, which, properly speaking, do not form granulations, but only spots which are not elevated, are due principally to the opacity of a certain number of convoluted tubes, the epithelium of which has undergone an advanced fatty transformation, while other groups, less altered, have preserved a relative transparence; this fact is well shown by one of the plates in Mr. Dickinson's work.[1]

The lesions, as you perceive, affect principally, in intersti-

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[1] *On the Pathology and Treatment of Albuminuria.* London, 1868. Pl. 2.

tial nephritis, the region of the labyrinth. At the same time the medullary substance is not entirely unaffected, but the modifications it undergoes are relatively less profound. The most striking feature of them is the tortuous direction, already

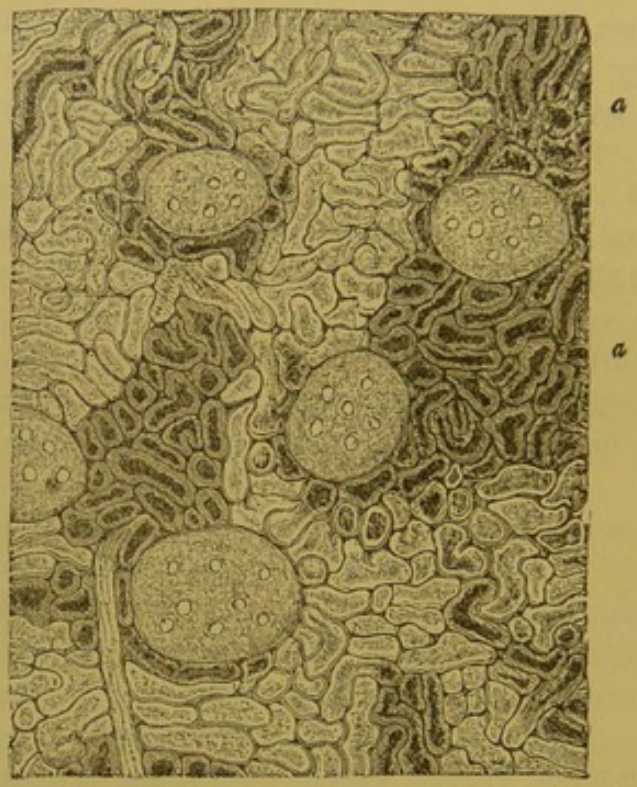

FIG. 16.—*Section of kidney affected by parenchymatous nephritis*, and in which the fatty degeneration is very extensive. The tubuli are not obstructed in a uniform manner; certain portions of these tubes, *a*, are distended and opaque, while others, *b*, are clear and translucid. The tubuli are all in immediate contact, in consequence of the absence of intertubular proliferation. (After Dickinson, Pl. II.)

mentioned, of the collecting tubes, the greater part of which have retained their epithelium, and the formation in their course, of cysts, which will be described hereafter.

III.

So far, gentlemen, our consideration has been confined almost entirely to the alterations which characterize the contracted kidney so far as they relate to the most advanced periods of the disease; it now remains for us to ascertain in what these alterations consist in the first stages of the malady.

We have not, on this subject, much information worthy of being utilized. This statement is easy enough of comprehension; in fact, *interstitial nephritis*, a disease primitively chronic, terminates in death usually only at the end of a very long period, and consequently the renal alteration is already of long standing. We can only hope, therefore, to observe the first phases of the changes in such cases where death has, so to speak, occurred accidentally, and, up to the present time, these cases have been rare.

Some authors complacently speak of a congestive period, and point out its characteristics, but this description is purely schematic. In reality, the few examples of incipient interstitial nephritis worthy of being utilized from the point of view we have assumed teach us what follows.

Macroscopically (Rindfleisch, Dickinson, Klebs), the volume of the kidney is normal, or but slightly hypertrophied; there are no granulations upon its surface; the capsule is easily removed. The cortical substance is slightly tumid; it presents a pale, grayish coloration, producing the aspect of parenchymatous nephritis. In certain cases, according to Klebs, the kidney is even very voluminous, and *renal cirrhosis*, like cirrhosis of the liver, would sometimes be preceded by real hypertrophy. In short, it would be, at this epoch, very difficult to distinguish interstitial from parenchymatous

nephritis, were it not for the histology which furnishes characteristics decisive of this period.

The histological study, in fact, enables us to recognize the following lesions :

1. From the commencement the connective stroma is infiltrated with a more or less considerable quantity of small, cellular elements, which, following the theory adopted, are called leucocytes or embryonic cells. To this cell-infiltration is due the grayish yellow color sometimes presented by the kidney at this stage of the disease (Rindfleisch). The anæmia here is only apparent; there is no compression of the vessels, and, contrary to what takes place in parenchymatous nephritis, these can be easily injected.

2. Another characteristic revealed by histological study is that, at this period, the tubular apparatus of the kidney presents no appreciable alteration ; the epithelium in the convoluted tubes is in its place, and perfectly healthy. The alteration of the epithelium is then a secondary event. In parenchymatous nephritis, on the contrary, the epithelium is the first affected, while the alteration of the connective stroma, if it occur, is consecutive.

As regards this point, there exists no difference of opinion among the great majority of authors who have separated the two forms of Bright's disease. Mr. G. Johnson has alone, for a long time, maintained, and still maintains (Brit. Med. Journ., 13th Feb., 1873), that, in the granulated kidney, it is the tubular epithelium which is the first seat of the alteration. According to him there is never, properly speaking, conjunctive hyperplasia in the so-called interstitial nephritis, this lesion being only a semblance of it, even in the phases of alteration the most advanced. The uriniferous tubes being deprived of epithelium and compressed upon themselves, produce here the resemblance of the pretended conjunctive hyperplasia. We have here an untenable thesis ; the oft-repeated confirmation of the infiltration of embryonic cells, in various stages of alteration, is enough to demonstrate the

existence of the formation of a conjunctive hyperplasia. English authors do not, indeed, dwell much upon this histological detail, so important in this case; that may, however, be owing to the method of preparation they have employed.

IV.

In the preceding studies I have endeavored more particularly to make you acquainted with the topography o the renal alterations in primitive-chronic-interstitial nephritis. This description is now to be completed by a work of analysis calculated to show the alterations undergone by each one of the elements composing the kidney.

A. As to that which concerns the connective stroma, I have little to add to what I have before said. *a.* The initial act is the formation of young cells which represents an embryonic tissue; this undergoes progressive organization, and soon assumes the appearance of fibrillar connective tissue. *b.* The new connective formation takes place particularly: 1st, about the convoluted tubes; 2d, about the glomeruli; 3d, about the principal vessels. *c.* The newly formed tissue is endowed, at a certain period, with the property of retractability, and to this property is due certain alterations that we shall have occasion to allude to hereafter.

B. The alterations of the *tubuli uriniferi* are produced only secondarily to those of the connective tïssue. *a.* The walls of the convoluted tubes are thickened, and tend to confound themselves with the circumambient tissue. *b.* The epithelium of these tubes undergoes fatty granular degeneration, and disappears. It is replaced: 1st, by granular or waxy cylinders; 2d, by a lining of young cells, round or cubical, the nature of which is not well determined (see Fig. 15), which

sometimes completely fill the lumen of the tube (G. Johnson, Kelsch), and at others form in the interior of the tubes a regular covering of a single range of cells;[1] in such a case, when the small cells fill up the lumen of the canals, these last become difficult of recognition, upon section, from the embryonic tissue which surrounds them. *c.* The tubes in certain cases are flattened at different points to such an extent that it is difficult to recognize them; at other times they are dilated here and there.

There are several varieties of these dilatations; sometimes the dilated tubes, varying in number, still preserve their epithelium; they may be voluminous, tortuous; in some cases they have lost their epithelial covering, which is replaced by waxy matter; finally, in certain cases there are real cystic dilatations. These dilatations may result: 1st, from pressure exercised upon a limited portion of the tube by the surrounding connective tissue; 2d, from the partial obliteration of the tube by a waxy cylinder; sometimes, indeed, as is seen in a plate by Cornil and Ranvier, the waxy cylinders may be distinguished in the midst of the colloid matter which fills the cyst.

These cysts are most frequently formed at the expense of the *canaliculi contorti*, and may cause prominences on the surface of the kidney, in some cases the size of a pea, though they are usually much smaller. They constitute by their presence one of the most constant macroscopic characters of interstitial nephritis, and are not found upon the large white kidney. The straight tubes in the medullary substance, in the neighborhood of the papillæ, are also sometimes found to be dilated and tortuous. The cysts of the medullary substance are sometimes ovoid, lengthened, and placed one above the other along a collecting tube, so as to resemble a

[1] This invasion of the convoluted tubes of the kidney by round or cubical cells calls to mind what occurs in the biliary capillaries in certain forms of cirrhosis of the liver, and in the walls of the alveoli or alveolar canals of the lung in certain forms of subacute or chronic broncho-pneumonia.

string of beads (Rindfleisch, Dickinson). Finally, in the cortical substance is found a third variety of cysts, formed at the expense of the Malpighian bodies; represented by Dickinson, they appear also to belong to the class of cysts by retention. The capsule of Bowman is dilated, and more or less distended by a colloid substance; its walls are thickened; as to the glomerulus, it is in such a case atrophied and pushed back upon a point of the wall.

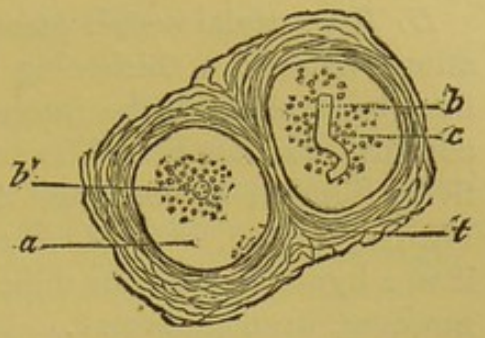

FIG. 17.—*Section of two cystic uriniferous tubes filled with colloid matter, a,* in the midst of which are seen hyaline casts of the same nature, *b b'* (Cornil and Ranvier).

C. The capsules of Bowman, aside from these cystic formations, show changes which merit special mention: 1st. At an early period there is simply thickening of the capsule, which seems composed of several concentric layers; the glomerulus which occupies the centre is healthy or sometimes hypertrophied; it escapes destruction for a long time, a fact to which prominence should be given from a pathological and physiological point of view. Later, however, the connective tissue of the glomerulus undergoes the embryonic transformation. This alteration recalls the scarlatinal glomerulus of Klebs, with this difference, that it is here a question of an affair of slow development, but, like the latter, its effect is to limit the circulation in the glomerulus. 3d. Finally, at a more advanced period the glomerulus has undergone the fibrous transformation; its form still exists in outline, but presents a vitreous, hyaline appearance, and is scarcely colored by carmine; the blood no longer penetrates into it, and the thickened capsule is immediately applied upon the glomerulus (Klebs, Kelsch), so as completely to efface the cavity. Lastly, I should remind you that in consequence of the giving way of the connective tissue of the labyrinth, the glomeruli are brought near together, and are, as it were, piled up

against each other (Dickinson), and that on the other hand, even in case where the changes are greatly advanced, some of the glomeruli are always found healthy and capable of performing their functions.

D. The arterial vessels present a special and constant alteration; namely, a thickening by concentric layers resulting from hyperplasia of the internal tunic, and particularly from adventitious deposit. The walls of the vessel appear relatively thickened, even when its lumen is greatly contracted. Mr. G. Johnson, who first described this alteration, attributed it to a hyperplasia of the muscular fibres; this detail has not, however, been confirmed.

LECTURE V.

CONTRACTED KIDNEY (*Interstitial Nephritis*).

Summary:—Characters of the Urine; Polyuria, Explained by the Excess of Tension.—Hypertrophy of the Left Heart without Valvular Lesion.—Albuminuria but Slightly Marked.—Urea in Normal Proportion.

Uræmic Accidents Observed in Interstitial Nephritis:—A. Chronic Uræmia; Dyspepsia; Amaurosis; Nervous Phenomena. B. Acute Uræmia.—Mechanism of Uræmic Accidents; Influence of Moral Emotions, Fatigue, Fever, Acute Lesions of the Heart, etc.

Disturbances in the Secretion of Uric Acid:—In the Gouty Kidney; in the Saturnine Kidney.—Difficulties of Elimination of Odorous Substances and Medicines.

Complications Observed in the Contracted Kidney:—Inflammatory Diseases; Coexistence of Interstitial Inflammations in other Organs (Fibroid Diathesis).—Alterations of Vessels; Atheroma of Arteries; Hemorrhages.—Lesions of the Retina.

GENTLEMEN:

I.—It is now time to endeavor to ascertain to what extent the minute study we have just made of the lesions of the kidney in the first variety of Bright's disease, is available in throwing light upon the mechanism of the functional derangements which characterize it clinically. I will at first confine myself to the modifications presented by the urinary secretion.

1. One of the most singular phenomena, and which has been remarked by all observers, is, that at an epoch which may be styled the period of *Status*,[1] not only is the quantity of urine not diminished, but it is increased generally above the normal average, a circumstance which offers a striking con-

[1] Meaning the second stage or fully developed state, or that of the highest development.—TRANSLATOR.

trast with what is met with in parenchymatous nephritis, in which the urine is more or less diminished. Dickinson has observed 2,700 c. c.[1] in the twenty-four hours, and Bartel has seen in one case the quantity augmented to five or six litres each day.[2] Thus the patients have a frequent desire to urinate, a fact of interest in enabling us to form a diagnosis.

To what is this exaggeration of secretion due? This is a question that has greatly exercised the sagacity of physiologists, but which does not seem to me to have been very satisfactorily answered. It is generally admitted with Traube, that in such of the glomeruli as continue to act (the quantity of blood remaining always the same), the pressure of the blood upon the arterial walls and its rapidity would be relatively great: this would result in additional labor by the glomeruli; and on the other hand, the momentary excess of water in the blood resulting from the renal impermeability, produces in the entire arterial system a condition of tension which, so long as the heart continues to act with energy, contributes still more to this supplementary elimination. I understand easily from this explanation why a sufficient quantity of urine continues to be secreted, but comprehend less easily why it is habitually *increased*.

Be the explanation what it may, it is to the augmentation of the arterial tension that is attributed, theoretically, the *hypertrophy of the left ventricle* without valvular lesion, which often accompanies interstitial nephritis.

The actual existence of this complication, already recognized by Bright, no longer needs to be discussed. The fact is the more worthy of mention, as this hypertrophy is almost never seen in cases of parenchymatous nephritis. Mr. Dickinson states that he never has met with it in these. In interstitial nephritis, on the contrary, it is met with in thirty-one

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[1] About 88 ounces.—TRANSLATOR.

[2] 165 to 198 ounces.—TRANSLATOR.

out of sixty-eight cases; according to Traube, in ninety-three cases out of one hundred, and according to Mr. Grainger-Stewart it is never, at a somewhat advanced stage, entirely absent.

This hypertrophy of the heart is said to be the result of the renal obstruction; if this, however, be the case, why is it not observed in parenchymatous nephritis, in which the embarrassment of the circulation is strongly marked, in consequence of the vessels being compressed in the cortical substance? To this question, theory answers: that persons affected by parenchymatous nephritis are debilitated subjects, in whom, for various reasons, and particularly on account of the great loss of albumen, the nutrition is profoundly affected, the nutrition of the heart being equally so with the other organs; in interstitial nephritis, on the contrary, nutrition continues normal for many years, and as the disease is developed in a very gradual manner, there is all this time for the hypertrophy of the heart to be brought about; such is not the case with parenchymatous nephritis, where, in consequence of the comparatively rapid progress, the equilibrium is quickly destroyed.

To this energetic action of the heart, which is characterized anatomically by hypertrophy of the left auricle and ventricle, and the physiological result of which is the persistence of the secretion of a considerable quantity of water by the kidney, is probably due this remarkable fact, that in interstitial nephritis dropsy is a very rare phenomenon, while in the large white kidney it is usual. You remember that Johnson, in twenty-six cases of the large white kidney, found dropsy in twenty-four, while in thirty-three cases of contracted kidney dropsy was observed only in fourteen cases. In the contracted kidney there existed most frequently a little puffiness, and œdema of the conjunctiva, known by English authors as "Bright's eye." (Grainger-Stewart).

In fact, this exemption in contracted kidney is peculiar only to the middle stages of the disease, since, at an advanced

period, when the heart becomes enfeebled by the general giving-out of nutrition, the urinary secretion is limited, or, rather, the kidney becomes more and more impermeable, and in such a case dropsy may occur, as in the large white kidney.

2. A second peculiarity of the urine in primitive interstitial nephritis is that it contains, contrary to what takes place in parenchymatous nephritis, only a relatively small proportion of albumen. Even this albuminuria is not always constant, but may be lacking from time to time; in the majority of cases—indeed, at the commencement of the disease, it occurs only temporarily; this fact Mr. Johnson has observed in chronic gout, in which albumen makes its appearance during the gouty paroxysm, and disappears in the intervals. Thus, Rayer said that gouty albuminuria presented less danger than other forms, while, in reality, it is a question of a grave disease, since death is sooner or later sure to ensue from it, though it leaves the patient a longer respite than parenchymatous nephritis.

This characteristic, deduced from the slight increase of albumen in this form of Bright's disease, has been observed by all writers who have distinguished the two varieties, and has served to render this distinction still more clear. It enables us to understand how, in parenchymatous nephritis, the nutrition of the system undergoes much more rapid changes than in interstitial nephritis, since in the latter the daily loss of albumen is much less. Thus, in a case of large white kidney, Bartels found a daily loss of fourteen to twenty grammes, while, in three cases of contracted kidney, he observed only one gramme and three-tenths; one gramme and two-fifths; one gramme and one-fifth—figures relatively insignificant.

What is the physiological cause of the presence of albumen in the urine in cases of interstitial nephritis, and why is it passed in such small quantity, while it is so abundant, on the contrary, in parenchymatous nephritis? This is a very im-

portant point to resolve, but of which we have no satisfactory solution.

I will only say that, according to all appearances, the mechanism differs here from that in parenchymatous nephritis. In the interstitial form the albuminuria does not depend upon the activity of the renal parenchyma; it is simply the effect of the excess of tension in the arterial system of the kidney; we know, indeed, that, under a feeble tension, colloid substances do not traverse the membranes, while upon more powerful pressure they are thus diffused, at least to a limited extent. Thus is produced, by the sole effect of arterial tension, the albumen in interstitial nephritis.

3. A third fact to be noted in the study of the urinary secretion in interstitial nephritis is the almost constant persistence, during the period of *status*, of the average amount of urea. Thus Bartels found, in several analyses, that about thirty grammes of urea were voided in twenty-four hours, while other analyses, made with reference to cases of parenchymatous nephritis, showed the daily amount excreted did not exceed thirteen to twenty grammes. The contrast is striking, and the more so since, according to all the authors who endeavored to establish between these two forms of Bright's disease a marked distinction, the phenomena conventionally styled *uræmic accidents* are much oftener observed in interstitial than in parenchymatous nephritis.

II.

I have just referred to the marked predominance of uræmic accidents in the interstitial form of Bright's disease.

A. It is especially in subjects suffering from interstitial nephritis that we meet with the varied and generally insidious

nervous accidents known under the name of *chronic uræmia.* Without entering in detail upon the varieties they may present, I will mention only certain ones.

1. There is at first habitual dyspepsia, frequently accompanied by persistent vomitings, which occur quite irrespective of food. In a number of instances an analysis of the substances vomited has shown them to contain urea or carbonate of ammonia.

2. Often, also, there exists a violent itching of the external cuticle (Bartels).

3. An interesting symptom of this kind of poisoning is *uræmic* amaurosis. This title should be reserved, as I have for a long time stated,[1] to characterize those disturbances of vision in Bright's disease which do not during life manifest themselves by any alteration appreciable by the ophthalmoscope. These occurrences are certainly rare in comparison with those which arise from a lesion of the retina; thus, according to Graefe, in thirty-two cases of amaurosis in Bright's disease, two only were uræmic; Mr. Badar, at Guy's Hospital, observed six cases of amaurosis *sine materiâ* out of thirty-eight cases of albuminous amaurosis. But, if infrequent, these accidents are sufficiently characteristic; aside from the retinal lesions appreciable by the ophthalmoscope, they are noticeable: 1st, by the rapid invasion of blindness; 2d, by its rapid disappearance; 3d, by its frequent returns. In the intervals between the attacks the vision may regain its normal acuteness; but after several attacks it may happen that amblyopia may become permanently established. This form of amblyopia is often only a precursory phenomenon, often followed by encephalic disturbances of a more serious nature (Gr. Stewart).

4. A peculiar headache, remarkable from its persistence, often exists; sometimes vertigo, drowsiness.

5. In other cases there are shocks, or subsultus in the

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[1] *Gazette hebdomadaire*, Tom. V., 1858, pp. 150 and 153.

limbs; sometimes a genuine tremor, such as exists in *paralysis agitans*, and which I have known in one case to continue several weeks without being accompanied by any cerebral trouble; uræmic encephalopathy, at first delirious, then comatose, terminated the scene.

The phenomena I have just enumerated are of so much the more interest, inasmuch as, until they are observed, the kidney affection is often undiscovered; the nervous accidents in question are sometimes, then, the first revelations of the disease, the urine upon the supervention of these symptoms being for the first time subjected to examination.

B. Uræmic accidents may still further be met with in interstitial nephritis, under an *acute form* presenting unusual peculiarities: 1st. A person, having in other respects all the aspects of health, is suddenly seized—for example, after bodily fatigue—with an attack characterized by *apoplectic symptoms*, which in some cases have led to the suspicion of opium-poisoning, or cerebral hemorrhage (R. Bright). 2d. At other times genuine *epileptic* attacks are observed, and these attacks recur a number of times before the appearance of permanent definite symptoms (Grainger-Stewart, Bartels). Finally, it is in interstitial nephritis that we have an opportunity of observing the phenomenon of the *skin covered with a white coating* of a crystalline appearance, and which analysis has shown to be composed of urea.

How does it happen, gentlemen, that we find this frequency and variety of uræmic accidents in a disease where generally the average amount of urea excreted in the twenty-four hours does not vary much from normal physiological conditions? Such is the question to be resolved at present. It must be remembered that the almost normal elimination of urea which takes place in interstitial nephritis is the result of a function to some extent supplementary, the accomplishment of which may be disturbed by the slightest influence.

The obstacle to the renal circulation has determined a per-

manent increase of tension in the arterial system; the heart has adapted itself to these new conditions, and become hypertrophied; as a result the water is excreted by the urine in an abnormal amount, carrying with it a sufficient quantity of urea. The equilibrium is thus re-established, but it is, so to speak, an unstable equilibrium, and easily destroyed. If, for example, a moral emotion supervenes, having the effect of momentarily lowering the heart's energy, the secretion of water becomes insufficient, the excretion of urea remains below the normal average, and the urea, as well as the other principal extractives, remain in the blood. Besides, this accumulation is so much more considerable in proportion as the subject affected previously possessed all the attributes of health—alimentation being abundant, bodily exercise normal, and consequently all the conditions existing for the production of a large amount of urea. Corporeal fatigue acts, in such a case, in the same way as moral emotions.

The mechanism by which these accidents are produced may be more complex: thus, a woman affected by interstitial nephritis, and in whom the equilibrium had been previously maintained, became affected with acute endocarditis; the mitral insufficiency resulting therefrom had the effect of diminishing the cardiac pressure; in addition to this, the presence of the fever produced an abnormal amount of urea, which, being imperfectly excreted, accumulated in the blood; as a result in this case, death rapidly ensued, with uræmic symptoms.

In all the circumstances which have just been mentioned, the appearance of uræmic phenomena in the course of interstitial nephritis is, so to speak, an accidental circumstance, proceeding altogether from increase of the proportion of urea, and from the diminution of the power of the heart. It may be asked if the accumulation of a large number of hyaline or waxy casts retained in the uriniferous tubes may not sometimes determine the production of uræmia. Bartels has examined the urine of subjects affected with interstitial ne-

phritis and suffering from uræmic symptoms, and has recognized in these cases an absence of casts.

In the advanced stages of the renal alteration, on the contrary, the appearance of renal accidents is an event necessary and fatal. If, in fact, the secretion of water and the excretion of urea can still go on in the kidney, even when it seems to be much altered, it is because some of the glandular portions have preserved their physiological structure; the moment arrives, however, when these parts, heretofore respected, are in their turn profoundly affected, and from this moment, the urinary function being by this circumstance considerably restrained or even suppressed, uræmic accidents occur with fatal effect. From this it may be understood that uræmia is the natural termination of interstitial nephritis. We shall soon perceive that the conditions in parenchymatous nephritis are wholly different.

III.

Having now become familiar with the modifications which take place in interstitial nephritis in the excretion of *urea*, we have to investigate the changes that occur relative to *uric acid*. This is a subject, so far, but little studied; still we possess some data which go to establish the fact that, even under circumstances in which the excretion of urea persists, that of uric acid is profoundly affected.

1. You are aware that, in chronic gout, according to the observations of M. Garrod, as well as my own, the kidney almost constantly presents the alterations of interstitial nephritis; the *gouty kidney*, according to M. Garrod, differs from that of ordinary interstitial nephritis only by the presence in the papillary portion of the pyramids of crystalline, tubular infarctions of white urate of soda; according to my

observations, even the presence of these crystalline deposits is not essential.

The first symptom which reveals the existence of this affection in gouty subjects is the occurrence of slight albuminuria, which, in the beginning, shows itself only at the time of the paroxysms, but which, sooner or later, becomes permanent. The very interesting observations of Mr. Garrod show that, at this period, while the excretion of urea remains normal, that of uric acid is already considerably limited. Thus the clear and abundant urine voided in the twenty-four hours by subjects affected by chronic gout contains, on an average, whether during the paroxysm or the interval, .064 gramme of uric acid, a proportion greatly below the physiological amount—.50 gramme.

It is also shown that the uric acid, in such a case, accumulates in the blood in the form of the urate of soda, and this seems to be, in part at least, the cause of the tophaceous deposits which, in subjects affected by chronic gout, are formed in abundance in and about the joints and upon various portions of the body.

2. The observations of Mr. Garrod tend to establish the fact, on the other hand, that lead-poisoning, like gout, affects especially the kidneys, and determines in them, before any other alteration, a limitation in the secretion of uric acid. Apparently this impermeability of the kidney to uric acid observed in lead-poisoning is the first sign of anatomical alterations, which later become apparent by the characteristic peculiarities of interstitial nephritis. Nothing, in fact, is more clearly shown than the frequent existence of granular nephritis in those suffering from lead-poisoning. This fact, to which a prominent place is accorded among us by Ollivier and Lancereaux, seems well established by English statistics: thus, in forty-two men affected by lead-poisoning, of whom autopsies were made in St. George's Hospital, Dickinson found contracted kidney in twenty-six. It is probable that to this special action of lead upon the kidney, the first effect

of which is to bring about retention of uric acid in the blood, is due the frequency of tophaceous gout in saturnine subjects. This coincidence remarked by Garrod has been also established by my own observations, and afterwards by MM. Potain, Bucquoy, etc. The gout of saturnine subjects, from what I have seen, appears to differ from ordinary gout only in the greater rapidity of its evolution, the abundance of tophaceous deposits, and the necessary existence, so to term it, of renal lesions.

From the above, it seems to result that the kidney, while yet remaining permeable to urea at a certain degree of interstitial nephritis, does not continue so to uric acid ; the same thing takes place with regard to certain medicaments, and this is a circumstance the practitioner should be careful not to forget. It has been long noticed that certain odorous substances do not pass into the urine of subjects affected with interstitial nephritis. One of the first observations of this kind is that of Halm, cited by Guilbert ; the case being that of a gouty subject, who took preparations of turpentine, and whose urine had none of the violet odor ; similar observations have been made by M. de Beauvais.

To this fact may be attributed the strongly-marked intolerance to opium which exists in subjects affected by interstitial nephritis ; administered even in feeble doses (0.25 centigramme of Dover's powder, Dickinson, p. 162), opium sometimes produces fatal comatose symptoms, probably uræmic ; it seems to act in this case especially by limiting the renal secretion. It has also been remarked by several English authors that in the same subjects the administration of small doses of calomel is very rapidly followed by profuse salivation and grave stomatitis.

These peculiarities have been pointed out thus far only with reference to interstitial nephritis, and are without doubt the consequence of anatomical modifications undergone by the kidney, but I would not venture to assert that they might not be produced in parenchymatous nephritis.

IV.

The more or less imperfect elimination of the products of renal secretion in individuals, the subjects of interstitial nephritis, has the effect of engendering in them an alteration in the crasis of the blood which renders them liable to contract certain inflammatory diseases. Bronchitis, next pericarditis, and finally pneumonia and endocarditis are, according to statistics, the inflammations which supervene most commonly in these subjects. Visceral inflammations are also frequent in parenchymatous nephritis, but, what is remarkable, do not affect the same organs. According to the statistics of Mr. Dickinson, the most frequent in this last affection are pneumonia and pleurisy; pericarditis being least likely to occur.

Another special trait in interstitial nephritis is the frequent coexistence of interstitial inflammations in other organs; thus, according to Grainger-Stewart, cirrhosis of the liver was observed in fifteen cases out of one hundred, and according to Dickinson in one case in seven; thickening of the capsule of the spleen and of the connective tissue of this organ was met with in forty cases out of one hundred.

Without admitting the existence of a fibroid diathesis, conjectured by Mr. Sutton, I should recognize the fact that in five or six cases of chronic interstitial pneumonia (fibroid phthisis of Sutton), observed at the Salpêtrière, I have twice seen interstitial nephritis with albuminuria; and even though atrophic alteration of the kidney is of frequent occurrence in old people (senile kidney), this does not produce albuminuria, which is very rare in old age, and in the two cases I speak of it was really an affair of interstitial albuminous nephritis—very different, anatomically and clinically, from the senile kidney.

To complete the consideration of the visceral complications which may supervene in interstitial nephritis, it remains to mention the *alterations in the vessels* which are found at the autopsy of such subjects as have succumbed to this affection.

Chronic endoarteritis or *arterial atheroma* is one of the lesions most frequently met with in these subjects; it is considered a consequence of the hypertrophy of the heart and of the increased tension to which the blood in the arterial system is subjected.

Correctly or incorrectly, to these alterations of the vascular system are readily attributed the *hemorrhages* which are frequently met with in the course of primitive interstitial nephritis. These hemorrhages take place in the most diverse ways: *epistaxis*, according to Rayer, is often one of the phenomena which precede and announce uræmic poisoning; at other times *hæmatemesis*, or *uterine hemorrhage*, will be met with (West); but of all the hemorrhages connected with interstitial nephritis, the most interesting and important are those which occur in the substance of the *encephalon*. There is no doubt but that a considerable number of the subjects of interstitial nephritis succumb from the existence of this complication, which does not belong to the history of parenchymatous nephritis.

Many authors consider it a simple solution to attribute the production of these intracephalic hemorrhages to the friability of the arteries and the increase of arterial tension. I am not prepared to contradict them on this point, and I believe, indeed, that the exaggeration of arterial tension contributes greatly to the development of these hemorrhages; but I must differ in opinion from those persons who believe that, aside from Bright's disease, atrophy of the kidney, combined with arterial atheroma, and perhaps with cardiac hypertrophy, is the ordinary cause of the majority of intracephalic hemorrhages in old people. I am able, indeed, to oppose to these assertions the statistics resulting from the extensive observations I made with M. Bouchard. Out of forty-nine

cases of cerebral hemorrhage, in sixteen only did the kidney present a certain degree of atrophy, and it must be especially remarked this was senile atrophy, common in old people; in none of them was there interstitial nephritis with albuminuria. No more is atheroma of the arteries of the encephalon the rule in our statistics, at least in arteries of a certain calibre; we find it indicated only in twenty-two cases out of one hundred. Hypertrophy of the heart is observed in twenty-two cases out of fifty-five. The essential element, in fact, which predominates above all in the production of cerebral hemorrhage, is the existence of miliary aneurisms, and the development of these aneurisms is not necessarily connected with renal atrophy, hypertrophy of the heart, or atheroma of the large vessels. I should add that in some cases of intra-encephalic hemorrhages, occurring in the subjects of interstitial nephritis with albuminuria, we have confirmed the existence of miliary aneurisms.

It seems to me incorrect to attribute, without question, to the atheromatous alteration of the arteries the retinal lesions frequent in this form of Bright's disease, and in a measure unknown in parenchymatous nephritis. I mean those lesions known by the name of albuminous retinitis, that is, the white plates, variegated by small hemorrhagic striæ, which are situated in the retina, particularly in the neighborhood of the papilla; so characteristic are these alterations, when well developed, as to be sufficient of themselves to establish the diagnosis of interstitial nephritis. Were this lesion really due to endoarteritis, it would be more frequently met with in old people, in whom arterial atheroma may be said to be common; it is, however, not observed in these conditions. I will limit myself to pointing out the frequency of this retinal lesion in interstitial nephritis, without being able for the moment to determine the physiological cause of its development.

LECTURE VI.

LARGE WHITE KIDNEY (*Parenchymatous Nephritis*).

Summary:—Synonym.—Two Varieties: Acute and Chronic.—Chronic Form.—Macroscopic Examination: Cloudy Tumefaction of the Epithelium; Dilatation of the Convoluted Tubes; Fatty Infiltration.

Morphological Varieties: Large Fatty Kidney; Fatty Granular Kidney; Small Fatty Granular Kidney.

Clinical Characteristics: Manner of Debut and Etiological Conditions.—Urine Scanty, Highly Albuminous.—Dropsies; Cachexia; Complications; Course and Duration.

GENTLEMEN:

We shall to-day enter upon the study of that variety of Bright's disease commonly designated under the name of *parenchymatous nephritis.*

This title presents a serious inconvenience; it involves, indeed, an hypothesis which is not yet demonstrated, namely, the inflammatory nature of the alteration. The same criticism may be applied to other terms proposed as synonyms: *tubular nephritis* (Dickinson); *non-desquamative nephritis* (G. Johnson). But, on the other hand, all these denominations perpetuate a fact which seems well established: it is that in the affection in question, contrary to what occurs in the form we have previously studied, the lesion localizes itself in the beginning in the tubular apparatus upon the epithelium; the connective tissue is spared, or affected only secondarily.

Other designations relate only to the appearances presented by the altered organ to the eye; in England, what we call here parenchymatous nephritis is often known by the name of "*large white kidney*" (Goodfellow, Wilks, etc.), "*large smooth kidney*," "*Bright's kidney.*" I confess that I have a

weakness for these entirely practical terms, which involve no hypothesis, and my predilection will doubtless seem to you justified when you learn that, in more than one respect, the histology of parenchymatous nephritis is still enveloped in profound obscurity.

I.

We generally recognize in parenchymatous nephritis two varieties, quite distinct from a clinical point of view: 1st, an acute form; 2d, a chronic form. I shall consider here only the *subacute* and *primitive chronic* forms.

One of the representations of Dr. R. Bright presents you with a perfect type of the alteration designated by the name of *large white kidney*;[1] the case was that of a drover by the name of Izod; this man, of dissipated habits, frequently became inebriated with porter, but the latter part of his life had used spirits. A year before, he had had an attack of dropsy, but his present illness had existed seven months; at this period the unfortunate man, while intoxicated, got wet, and dropsy rapidly supervened; death appeared to have been produced by pulmonary complications.

The autopsy showed the kidneys to be white, voluminous, and smooth; the lungs were œdematous. We have in this case, in some degree, a classical history. Let us now examine more precisely the renal alterations that are met with in cases of this class.

A. Macroscopic examination.—The kidney is large, often

[1] R. Bright: *Report of Medical Cases*. London, 1827. Case XI., p. 25, plate IV., Figs. 4 and 5. See Plates I. and II. See also plate annexed to the work of J. Osborne: *On Diseases connected with Suppressed Perspiration and Coagulable Urine*. London, 1835.

being twice its normal weight and volume. The color is white—sometimes a dead white, resembling more or less that of ivory—sometimes having a more or less yellowish tinge; this coloration belongs exclusively to the cortical substance of the kidney; it is observed upon the surface of the organ after having removed the capsule, which is nowhere adherent to it; at the same time we find the surface to be absolutely smooth, presenting neither prominences nor cysts, such as are found in the granular kidney, nor are depressions ever found other than such as separate the large, natural lobes; even the lobular structure of the kidney, as it is found in a normal state marked by vessels, is here effaced; the vessels are seen here and there only in the form of spots disseminated at wide intervals. Upon section, the considerable tumefaction of the cortical substance and the rarity of vascular striæ are recognized.

The medullary substance shows no appreciable alteration; its color varies but little from that of the normal state, and presents a more or less striking contrast to that of the cortical substance.

B. Histological study.—When this form is encountered in all its purity, the alterations are localized almost exclusively in the convoluted tubes, and in these—the epithelium remaining *in situ*—present, in the majority of cases, modifications so slight that they deviate from normal conditions only by shades of difference. Nothing less than a practised eye suffices to recognize them.

a. In the first degrees nothing is perceptible more than a *cloudy tumefaction* of the epithelium. The glandular cells of the convoluted tubes, more sombre than in a physiological condition (in consequence of the presence of a very large number of fine granulations), are at the same time more voluminous, and swollen to such an extent that the lumen of the canals is found contracted; often, also, though not invariably, the free portion of the tubes is obliterated by fibrinous cylin-

ders. Otherwise no appreciable lesion is found to exist in the connective stroma nor in the vascular tunics.

You perceive that it is, as I announced, only a question of simple shades, of a sort of exaggeration of normal conditions, for you have not forgotten that, in these conditions, both in the living animal and in the healthy man, the glandular epithelium of the convoluted tubes presents a sombre hue and numerous granulations, and that the lumen of these tubes is naturally reduced to a very small size. It is not remarkable, then, that some authors, particularly Mr. Gairdner, to whom we are indebted for one of the first works upon the subject, should have been led to declare that the results of histological investigations are, in such a case, so to speak, negative. The tumefaction of the epithelial elements is, however, incontestable, and to this may even be mostly attributed the increase in size of the organ, often really enormous.

b. Besides the opacity of the epithelial cells, we also note as characterizing parenchymatous nephritis : a more or less pronounced dilatation of the convoluted tubes and varicose conditions of their external contour (Rindfleisch) ; also a certain thickening, sufficiently difficult, I think, to appreciate, of the proper tunic of these tubes.

c. There exist, in this degree, no signs of a multiplication or proliferation of epithelial elements. The straight tubes undergo no alteration. Such, however, is not the case with Henle's loops, the greater part of which, according to Cornil, present an alteration similar to that existing in the convoluted tubes.

2. The cloudy tumefaction of the epithelium may be the only alteration met with, even when death has not occurred till late (six months to a year) after the *début* of the disease, but it is often complicated with a genuine fatty infiltration of the cell-elements. These then contain, in addition to the protein granulations, minute globules, more or less voluminous, which resist the action of acetic acid, and are soluble in ether. The tubuli, whose epithelium is thus modified, appear

by a feeble magnifying power quite black and opaque; this modification, very different this time from the normal appearance, is presented by Henle's loops, but, above all, by the convoluted tubes.

a. Sometimes the fatty infiltration is uniformly diffused, and to the naked eye the ordinary appearance of the large

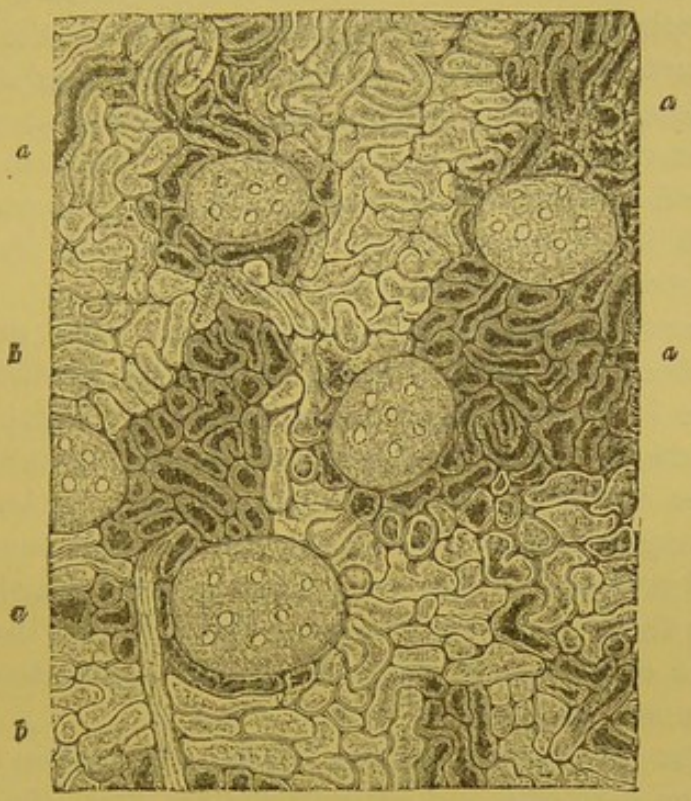

FIG. 18.—*Section of a kidney affected with parenchymatous nephritis*, and in which the fatty degeneration is greatly extended. The tubuli are not obstructed uniformly; certain portions of these tubes, *a*, are distended and opaque, while others, *b*, are clear and translucent. The tubuli are all in direct contact, owing to the absence of intertubular proliferation (after Dickinson, Pl. II.).

white kidney is but slightly modified. It has a yellowish tinge like buff leather, which takes the place of the pale, ivory-white appearance, but remains large and with a smooth surface void of granulations. This condition is sometimes known by the name of *large fatty kidney*.

b. At other times the fatty degeneration affects only certain groups of convoluted tubes here and there, the interme-

diate groups remaining in the first stage of alteration. These groups of *tubuli*, having become fatty, appear opaque by comparison with the others, and even form sometimes small tumefactions appreciable not only on the surface of the kidney, but, upon sections being made, in the thickness of the cortical substance. These granulations, you perceive, differ from those we have studied in the kidney affected by interstitial nephritis, for the latter exist only upon the surface, and are produced by the continuance of the medullary rays of each lobule. The macroscopic appearance corresponding to this alteration has been represented by Bright in his third plate,[1] and by Rayer in his eighth.[2] It is the fourth variety described by the latter author. Johnson calls the kidney thus altered the *fatty granular kidney*.

3. According to Mr. Dickinson and a large number of other authors, the fatty kidney, smooth or granular, represents the last stage of parenchymatous nephritis. There exists, besides, a certain number of facts which tend to demonstrate that in certain cases, rare indeed, the large white kidney may in time undergo a more or less pronounced atrophy, and present, in consequence, appearances which make it resemble those of the small contracted kidney, so that in such a case the separation established between the two forms might at first appear arbitrary.

This atrophic alteration of the kidney, consecutive to parenchymatous nephritis and entirely distinct from the atrophy produced by interstitial nephritis (contracted kidney, small granular kidney), is sometimes designated as the *small granular fatty kidney*. The consecutive atrophy in the case of parenchymatous nephritis seems to be effected by the following mechanism: the epithelium, after having become fatty, undergoes at certain points a real liquefaction, in consequence of which the fatty granulations become free; some pass into

[1] *Reports of Medical Cases*, Pl. III., Figs. 1, 2, 3.

[2] Rayer, *Atlas* in fol. du *Traité des maladies des Reins*. Paris, 1837. Figs. 1, 2, 5, and 6.

the urine, the others are reabsorbed, and it is under such circumstances, according to the observations of Beer, that the lymphatic spaces are filled with fatty granulations.

As a consequence, a certain number of tubes thus deprived of their epithelium become empty and collapse, while others, less advanced in the process of alteration, have not passed beyond the first phases of fatty granular infiltration. It does not appear that in general there is here any process of connective hyperplasia.

According to the observations of Mr. G. Johnson, the *small fatty kidney* may always be distinguished from the *contracted* kidney anatomically, and without considering the clinical history. Here is a summary *exposé* of the differential characters, placed in relief by this author :

The contracted kidney is of very small size ; it has a fibrous consistence ; the granulations are met with only on the surface ; they rest on a red vascular foundation, and never have the appearance of small steatosed masses ; finally, the surface of the organ is covered with cysts, which are also found in the deeper parts of the organ. On the contrary, the atrophied white kidney is never as small as the red cirrhosed kidney ; it is of less firm consistence ; its surface is always more uneven, indented, and nodose,[1] as Bright says ; the granulations are in some degree of a coarser character (G. Johnson) ; they exist in the deeper portion of the cortical substance, as well as on the surface ; they are yellow, and evidently formed by the accumulation of granulations and small fatty globules in the tubuli ; the general hue of the cortical substance is pale and yellowish, but slightly vascular, and not red, as in the contracted kidney ; finally, cysts do not ordinarily exist either in the interior or upon the surface of the organ.[2]

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[1] Motley and tuberculated appearance of the kidney.

[2] See upon this subject : G. Johnson, *On the Forms and Stages of Bright's Disease of the Kidney*, in *Med. Chir. Trans.*, Vol. XLII., 1853, with colored plates. I have lately had the opportunity of verifying in several instances the perfect ex-

Such, gentlemen, are the principal anatomical conditions connected with the variety of Bright's disease in question. You will sometimes be told that the appearances of the alterations as presented by the kidneys to the naked eye in Bright's disease, are so varied that they differ, so to speak, in nearly every subject. This is evidently an exaggeration ; we must always realize that these appearances are numerous; thus, besides the small red granular kidney (interstitial nephritis), we have the large, white kidney ; the large, smooth, fatty kidney ; the fatty kidney with granulations, and finally, the atrophied and granulated fatty kidney (small, granular fatty kidney). It is easy at all times, as you have just seen, to group all these varieties about two fundamental types, which two alone can be considered distinct species, having an autonomous existence.

II.

I hope I have succeeded in showing you, gentlemen, that in the anatomo-pathological relation there exists between interstitial nephritis and parenchymatous nephritis a clearly-marked line of demarcation. This demarcation also exists in the domain of clinical observation.

A. The *début* of the variety of Bright's disease, which is characterized anatomically by the lesions we have just described, generally takes place in a slow manner. There are exceptions to this rule, much less numerous, however, than some authors appear to believe. Thus you often hear that the lesion of the large, white kidney, with all its clinical con-

actitude of Mr. Johnson's observations relative to the distinctions to be established anatomically and clinically between the *small fatty kidney* and the *contracted kidney*.

sequences, has for its origin *scarlatina*, in the course of which it is developed in an acute manner ; but if we seek for proofs of this assertion, we shall nowhere find them. Scarlatinous nephritis is an affection by itself, which is evolved in a fashion of its own, and which, as we shall see later, resembles greatly in an anatomical point of view interstitial nephritis.

It is true that permanent parenchymatous nephritis sometimes commences like an acute disease, that is to say, suddenly, with the accompaniment of febrile action more or less pronounced, and more or less lasting. But we must recognize the fact that these instances are not numerous ; they seem to be met with oftener in England than almost anywhere else. Thus, Bartels says that in England he saw but one case of this kind ; Wilks, on the other hand, has collected four or five ; Dickinson nearly as many ; Bright has cited three that came under his observation ; I do not think there are many reported in the French publications.

All these cases seem to have the peculiarity in common of being contracted under the influence of cold, the body being in a perspiration. For example, in a case observed by Wilks,[1] a man, twenty-eight years of age, being heated and in a state of intoxication, threw himself into the Thames, and swam for some time ; the next day there was considerable anasarca and intense fever ; the urine was scanty and dark, and highly albuminous. The patient succumbed at the end of three months, in consequence of a gangrenous inflammation of the skin of the legs and scrotum, consecutive to punctures made for the purpose of evacuating the liquid of the œdema. At the autopsy the kidneys were found to be greatly enlarged, and to present already the characters of the large white kidney. All the observations of acute parenchymatous Bright's disease having an acute beginning seem made upon cases nearly identical.

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[1] *Cases of Bright's Disease, Guy's Hospital Reports*, 1852, twenty-three observations.

Aside from the influence of the action of cold, and leaving out of consideration the influence of scarlatina, which seems to have nothing in common with the development of the large white kidney, we are unable to designate, in the *etiology* of this affection, any determining condition. Much has been said of the influence of other diseases besides scarlatina, namely: measles, diphtheria, erysipelas, the action of certain remedies upon the kidney (cantharides, turpentine, copaiba, etc.). Under the influence of the preceding causes are, in fact, often produced albuminuria and a granular alteration of the epithelium more or less marked, but it has never been distinctly established that a permanent case of Bright's disease has ever been produced by such an etiology.

B. Be the cause what it may, whether the *début* be gradual or rapid, the *symptoms* in the period of status (second or fully developed stage—TRANS.) are always nearly identical.

1. The urine is *scanty*, and in the acute stage sometimes greatly diminished; under ordinary circumstances even, we find the amount in the twenty-four hours to be 500 or 600 grammes. This fact, which is in marked contrast with what is seen in interstitial nephritis, is so much the more interesting, as patients suffering from parenchymatous nephritis have an incessant inclination to urinate; they have, as the English say, *irritable bladder;* but if the urine passed in a given time be measured, the quantity is found to be very small. This scantiness of the urine is moreover explained: by the dropsy which is here an habitual phenomenon; by the anæmia of the cortical substance of the kidney, which is not in this order of facts the occasion of a work of compensation on the part of the heart; perhaps, also, by the abundance of urinary casts, which, in certain cases, at least, may act as tubular infarctions, and hinder secretion.

The proportion of *urea* is generally below the normal (15, 20 grammes). The existence in the dropsical fluid of a certain quantity of urea, and the diminished energy of the nutritive process, always constant in these ailments of a more

or less cachectic character, seem sufficient to explain this fact.

The excretion of *uric acid* seems to undergo no appreciable modification.

Albuminuria is strongly marked in this form of Bright's disease; some patients lose in the twenty-four hours fifteen to twenty grains of albumen; the urine then containing three per cent., that is to say, a larger proportion than exists in the serum of blisters.

2. Next in order to the characteristics afforded by the examination of the urine, the most prominent phenomenon is the dropsy; it may be said, in the form of Bright's disease we are studying, to be constant, and, in addition, often produces death either directly (hydrothorax, etc.), or by becoming the point of departure of various accidents; gangrenous erysipelas and phlegmonous swellings of a severe nature are more frequent in this than in all the other varieties of dropsy.

3. Inversely to what is observed in the case of contracted kidney, subjects attacked by parenchymatous nephritis rapidly grow cachectic and anæmic; the loss of a large quantity of albumen contributes decidedly to the production of this result.

These patients are dyspeptic, and often become subject to vomiting. According to Messrs. Fenwick (cited by Grainger-Stewart) and Wilson Fox, an intertubular gastritis is often produced in interstitial nephritis, and in parenchymatous nephritis, on the contrary, a special lesion of the follicles.

Finally, I will only recall to you the fact already mentioned, that hypertrophy of the heart, cerebral hemorrhage, albuminous retinitis, etc., do not belong to parenchymatous nephritis, or show themselves (according to some observations) only at the period of atrophy.

Death ensues as the result of various circumstances: I have already mentioned erysipelas of a grave character, and abdominal dropsies, which are the most common causes of a fatal termination. Visceral inflammations are not rare, particularly

pneumonia and pleurisy, pericarditis being next in frequency; some cases have also occurred of peritonitis dependent upon parenchymatous nephritis. Finally, uræmia may be met with, but much less frequently than in interstitial nephritis; it seems to be often developed in those cases in which large quantities of water are rapidly lost from the system by other outlets than the kidneys (Bartels), as, for instance, consequent upon copious diarrhœas provoked by purgatives, and still more after profuse sweats produced by vapor-baths, and which bring about a rapid reabsorption of dropsical effusion.

There is no doubt but that this disease is curable; it sometimes presents periods of amelioration, varying in the duration of their continuance, during which a certain quantity of albumen is always found in the urine; ameliorations which are often only temporary, and are soon followed by relapses. This condition of things may be prolonged five or six years, and it is then that the small fatty granular kidney, described by Mr. G. Johnson, is found upon autopsy; otherwise these cases are exceptional, and generally the duration of parenchymatous nephritis hardly exceeds a year, while interstitial nephritis may be prolonged during many years—as long as ten years, according to my observations.

LECTURE VII.

SCARLATINOUS NEPHRITIS.—AMYLOID KIDNEY.

Summary :—The Lesions of Scarlatinous Nephritis not those of Parenchymatous Nephritis, but rather those of Acute Interstitial Nephritis; they affect especially the Glomeruli.

Of Amyloid Degeneration in General.—Amyloid Substance : in the Vascular Walls ; Cellular Elements ; Hyaline Membranes.—Appearance.—Reagents.—Chemical Constitution.—Nature.—Etiological Conditions.

The Amyloid Kidney.—Histological Examination : Analytical Study of Lesions ; Study upon Sections of the Kidney.—Macroscopic Characters.

Clinical Phenomena.—Diagnosis Founded upon Extrinsic Considerations.

GENTLEMEN :

I hope I have said enough in the preceding lectures to establish the proposition I formulated in commencing this series of studies, namely, that the two varieties of Bright's disease, characterized anatomically, one as the *small granular kidney*, the other as the *large white kidney*, are as distinct clinically as they are from an anatomo-pathological point of view. I will terminate this series of lessons by presenting you some views relative to *scarlatinous nephritis*, and to the *amyloid kidney*.

I.

The history of *scarlatinous nephritis* is confounded by many authors with that of parenchymatous nephritis. In

studying this subject, not simply in connection with the *dicta* of systematic works, but going back to original documents, we are quickly impressed by this fact, that the opinion which makes scarlatinous nephritis the point of departure of permanent lesions attributable to the *large white* kidney is founded on no decisive observation. Doubtless there exist cases in which occur an acute febrile commencement, dropsies, and a continuance of two or three months, and in which an alteration is found upon autopsy, resembling that which characterizes the *white kidney* of parenchymatous nephritis. It is true that the diseased kidney may be augmented in volume, with a smooth surface, and its cortical substance, thickened, may present a yellowish tinge, or white mingled with red striæ. But we have already observed that in the first phases of interstitial nephritis the kidney offers a close analogy to the white kidney of parenchymatous nephritis, and in reality the few observations of *scarlatinous nephritis* in which a regular histological examination has been made concur in showing the renal alteration observed in such cases to be a form of acute or subacute variety of interstitial nephritis.

Thus, in a case studied by Mr. Biermer (*Arch. für path. Anat.*, XIX.), and in another of the same kind reported by Mr. Wagner (*Arch. der Heilk.*, 1867, p. 264), an infiltration of small cells was found to exist in the thickness of the connective stroma of the cortical substance; the epithelium was hardly altered; at all events, it was not infiltrated with fatty granulations; a remark already made by Mr. Dickinson, who, indeed, says nothing of conjunctive proliferation. Mr. Klebs, on his part, has described in certain cases of scarlatina a renal alteration, which he designates as *glomerulitis*, and which, as we have said, consists of a proliferation of the connective woof of the glomerulus.

Finally, Mr. Kelsch, in his important work, makes known the fact that in two cases of scarlatinous lesion of the kidney he was surprised to meet with all the characteristics peculiar to the first stages of interstitial nephritis—particularly infil-

tration of small round cells. In the cortical layer the uriniferous tubes were dissociated as if dissected, by layers of young embryonic cells; this alteration affected the entire thickness of the lobule, the labyrinth, as well as the medullary rays. The glomeruli were converted into an embryonic tissue formed of young cells closely confluent. The epithelium of the convoluted tubes was granular, but little swollen, the central canal of these tubes being free through its entire extent.

These are, perhaps, the only observations in which the histology of scarlatinous nephritis has been regularly observed, and they all concur in showing, as you see, that we have to deal with, not a first stage of parenchymatous nephritis, but decidedly, on the contrary, with an interstitial nephritis of rapid development. It does not appear that scarlatinous nephritis has ever culminated in the production of the contracted kidney.[1]

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[1] J. Coats has published in the *British Medical Journal* (Sept. 26, 1874) the following history of a case:

Y. R., aged twenty years, was admitted Sept. 30, 1871, to the fever wards of Dr. McLaren, in the royal infirmary of Glasgow. His illness had commenced five days before by a loss of appetite, pains throughout the whole body, headache, dysentery, difficulty of swallowing and nausea without vomiting; the eruption had made its appearance the second day of the disease, and covered, from the moment of its appearance, the trunk and limbs; the temperature in the axilla was 101° F. The patient was anxious, partially unconscious, and during the night had delirium. The fourth of October the eruption was still out upon the abdomen, and the temperature was 103.4° F. The patient died October 5th, five days after admission, and on the tenth day of the disease.

The autopsy was made twenty-seven hours after death. The size of the liver and spleen was considerably increased; the liver weighed five pounds, and the spleen twenty-one ounces. The mesenteric ganglia were swollen, and red upon section, and there were also redness and tumefaction of Peyer's patches and the solitary glands of the large intestine. The two kidneys, very voluminous, together weighed twenty-two ounces. To the naked eye they presented, in the most striking manner, the appearances of the large white kidney, the cortical substance being very pale and thick.

The *histological* characters were absolutely characteristic. The increase of volume and the pallor of the kidney were due to an almost general infiltration of

II.

It is a long time, gentlemen, since the alteration, designated by the name of *amyloid degeneration* of the kidney, was separated from the heterogeneous group comprised under the name of Bright's disease; it is true, indeed, that the renal lesion in this alteration presents characteristics sufficiently marked, and in the midst of very peculiar circumstances, which together entitle it to a separate classification.

The amyloid alteration cannot be said to have an *autonomous existence*. It is always subordinate to a constitutional state—to a disease which at the same time, in addition to the kidney, affects different viscera: the liver, spleen, intestine, etc.

A. These various visceral alterations, subordinated as they are to the same influence, all present, besides, one anatomo-

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the cortical substance by a multitude of round cells. These were diffused around the tubules, which they separated without the epithelium being notably altered; they were of the size of white blood-corpuscles, and were distended. The appearance just described was evident and easy to perceive on making a thin transverse section, particularly at the points where the epithelium was detached. The cells were so abundant that the section perfectly resembled a preparation in my possession, originating in a leucocythemic nucleus. In the case described, as in the preparation referred to, there is a clearly-marked intertubular infiltration, with this difference, that the infiltration exists, not simply at a limited point, but in the entire cortical layer. The epithelium of the tubuli is scarcely modified, or at most a little tumid and granular. Section gives an appearance closely resembling one of the plates in the *Histologie pathologique* of Rindfleisch (French translation, Fig. 196 (?), p. 516).

Thus we find here an acute interstitial nephritis, general in the two kidneys, supervening in the course of scarlatina, and terminating fatally the tenth day. I am not certain that an analogous case has been reported up to the present time; but, such as it is, it demonstrates, so far as evidence goes, the existence in the kidneys of acute interstitial inflammation.

pathological characteristic in common. This characteristic consists in the presence, in the midst of certain anatomical elements, of a substance endowed with special morphological and micro-chemical properties. The substance in question is commonly designated by the name of *amyloid substance*, but this title is quite incorrect, inasmuch as it contains nitrogen, and consequently, in this respect, varies as much from the cellulose of starch as it resembles albuminous substances.

a. The so-called amyloid substance is found, in the first place and principally, in the walls of the arterioles and capillaries; less frequently in the veinules; it is never met with in vessels of a certain calibre, and if discovered in the aorta, it should be remembered occupies only the *vasa vasorum*.

The altered parts of these vessels are generally increased in volume; they assume a homogeneous aspect, being transparent, vitreous, and opalescent, all the details of structure of the altered parts having a tendency to blend together and to become effaced.

The alteration first affects the internal membrane, which may be found to be the only affected portion; then the limiting membrane; later the muscular fibres of the middle tunic assume, in their turn, the homogeneous and vitreous appearance; last of all, though rarely enough, the adventitious membrane and the surrounding connective tissue may be also altered.

When the arterioles are thus affected they present a knotty appearance, which has led to their being compared to the roots of ipecacuanha (Grainger-Stewart). In the capillaries the alteration presents the same characters; the nuclei dissolve and disappear in the midst of the vitreous substance. The final result, to sum up, is a thickening of the vascular walls, which may lead even to complete obliteration of the lumen of the vessel.

b. The parenchymatous cells may also be invaded by the amyloid alteration; in the liver, for example, the hepatic cells are sometimes affected primitively, independent of the

arterioles; they are increased in size, disfigured, their contour is indistinct, and their angles blunted; their protoplasm is replaced by a vitreous, opalescent substance, which conceals the nucleus. It often happens, then, that the altered cells become confounded with each other. An anatomical alteration may be produced in the muscular cell-fibres of the intestine (Rokitansky), and in the cells of the subcutaneous connective tissue or of the mesentery (Hayem); in this last case the vitreous matter occupies the protoplasm in the neighborhood of the nucleus, and forces back the fatty matter.

c. The hyaline membranes—those, among others, which form the walls of the tubuli uriniferi—may participate equally in the alteration.

B. The parts affected by amyloid degeneration present a peculiar aspect—described, in 1842, by Rokitansky, by the name of *lardaceous appearance*. The diseased portion is anæmic, pale, yellowish or gray, slightly transparent, of a soft consistence and waxy feeling, preserving the impression of the finger. Amyloid degeneration is, however, seldom found entirely pure and disconnected from accessory elements; in the kidney, for instance, it is often coincident either with the lesions of interstitial or with those of parenchymatous nephritis. To recognize it, particularly at the commencement of the disease, the simple appearance—which may be deceptive—should not be too much trusted, but recourse to reagents is a matter of absolute necessity.

C. The reagent generally employed is *iodine*. The best to use is an aqueous solution of iodine, with the addition of the iodide of potassium, and having the color of dark sherry. If this solution be poured upon the parts affected by amyloid degeneration, the effect is to produce a general yellow color, in the midst of which striæ, or sometimes patches, are distinguishable, according as the vessels only, or the other elements, are affected by the degeneration; these striæ or patches have a mahogany color. If, then, upon the portion thus colored, a drop of sulphuric acid be applied, the reddish

brown color sometimes, but not invariably, changes to a blue or violet coloration, more or less deep.

For the purpose of demonstrating the amyloid alteration, other reagents are sometimes employed, as, for example, the ioduretted chloride of zinc. Mr. Dickinson has recently studied as a reagent the *sulphate of indigo*. When a piece of healthy kidney is suffered to remain for some time in a weak solution of this substance, the former becomes of a blue color, the blue tint soon disappearing, to be succeeded by a pale green coloration. When, on the contrary, a portion of an amyloid kidney is employed, the parts affected by the degeneration preserve for a long time a strongly pronounced blue color, which contrasts with the color of the portions that have remained healthy. It is understood that, in the histological investigation, the ioduretted reagent brings into clear relief the elements altered by the amyloid degeneration.

D. A word now relative to the *chemical constitution* of amyloid matter. I have already told you that it has nothing in common with cellulose and starch, with which the reaction of iodine caused it at first to be compared. The elementary analyses of Kekulé, Rudneff, and Schmidt, made of the amyloid substance of spleens thoroughly permeated by it, have shown nitrogen to be one of its elements. That it approaches in character to the amyloid substances is incontestable, but beyond this we know on this point nothing positive.

Recently Mr. Dickinson has essayed to go a step farther, and has promulgated the hypothesis that the amyloid substance is nothing more or less than fibrin deprived of the free alkali which enters normally into its composition.

He observes, in the commencement, that one of the characters of amyloid matter, when compared with other albuminous substances, is the absence of free alkali; thus, in an amyloid liver, the proportion of alkali (potash or soda) was one-fourth less than in a healthy liver.

The amyloid liver loses the property of being colored by iodine if previously macerated in an alkaline solution; this

fact leads to the supposition that amyloid matter is an albuminous substance deprived of alkali.

Another circumstance tends still further to establish the fact that this substance is only a modification of fibrine. This consists in the artificial preparation, by the aid of fibrine, of a substance which presents the optical and chemical characters of amyloid matter. Fibrine is dissolved in dilute hydrochloric acid (one ten-thousandth part); the fibrine is recollected by evaporation of the solution, but freed from alkali, and is found to exist in the form of a gelatinous substance, which presents in the most striking manner the reactions of amyloid matter. Mr. Dickinson founds thereupon a complete theory of amyloid degeneration, in which I will not follow him; but the facts which he has exposed being still but little known, I have thought it useful to mention them.

E. The amyloid degeneration, as I have already mentioned to you, affects *several organs simultaneously*, so that the renal, in this *ensemble* of alterations, is, so to speak, only an episode. The question, however, arises here: Is the infiltration of the affected tissues produced by a substance previously formed in the blood, or is the amyloid matter formed at the expense of pre-existing tissues? In the present state of science this question seems utterly insoluble; I content myself here with referring to it, only adding that thus far a study of the blood in subjects affected with the *lardaceous disease* has shown absolutely nothing which recalls the amyloid substance.

F. A study of the *etiological conditions* furnishes very important data; it generally establishes the existence of a concurrence of circumstances which vividly characterize the situation, and which justify us in suspecting almost always, when they are present, the existence of some one of the forms of amyloid alteration, particularly that of the kidney.

1. One of the most frequent of these circumstances is a *prolonged suppuration*, whatever may be its cause (caries, necrosis, diseases of the bone; Pott's disease with abscess;

phthisis, with vomicæ ; dilatation of the bronchial tubes ; dysentery, with abscess of the liver ; old ulcers of the leg). Suppuration of one of the kidneys has often brought about amyloid degeneration in the other (Rosenstein).

It is upon the predominance of this etiological condition, which is well confirmed, that the humoral theory of Mr. Dickinson is in part founded. The pus is a liquid rich in albumen and in alkaline salts ; the continuance of suppuration may, therefore, have the effect of depriving the blood of a portion of its albumen and alkalies ; the fibrin would thus become relatively predominant, but at the same time poor in alkaline matter, and this circumstance would lead to the formation of amyloid matter, which is, according to this author, only fibrine deprived of its normal free alkali.

2. *Albuminuria* acts in the same manner. This, indeed, whatever its origin, figures among the circumstances which preside at the development of lardaceous disease.

Without entering upon a critical disquisition of this theory, I would say that it is not capable of as wide an application as the author desires. There exist, indeed, other circumstances under which amyloid degeneration is produced, and where, nevertheless, there is no prolonged suppuration ; thus, in certain statistics, syphilis figures as a prominent cause ; there have been mentioned also as possible causes, *chronic articular rheumatism*, and various forms of *cancer ;* besides, it must not be forgotten that, in more than one case, the etiological condition remains quite in obscurity.

G. Amyloid degeneration may be observed at any age ; it has been known to occur at the age of two and a half years in a child affected with coxalgia ; it may, like scrofula, be met with up to the age of seventy years, but is most frequent between the ages of twenty and thirty, that is, during the period in which phthisis dominates.

III.

After this preliminary exposition devoted to the study of amyloid degeneration in general, it is in order, gentlemen, to enter upon the special description of the amyloid kidney. I will commence with an *exposé* of the histological lesions, with which I will then connect the macroscopic appearances. I would state at the commencement, that when the disease has reached the middle period of its development, the macroscopic appearances are especially those of the large white kidney, with a yellowish hue in certain cases; the distinction, however difficult at first, becomes easier when the intervention of reagents is brought to bear. All the parts touched by the iodided reagent are colored, but the particular mahogany coloration is localized in the cortical layer and upon the glomeruli; in the medullary substance it shows itself in the form of parallel striæ which correspond to the course of the straight vessels; the histological reason of this disposition we shall soon learn.

A. In the kidney, as in all other organs, the amyloid alteration is established primarily in the system of *arterioles:* the vessels of the glomeruli are affected first, the glomerulus being enlarged and presenting the special coloration under the influence of reagents. It is quite remarkable that all the glomeruli are not affected simultaneously, the lesion appearing first in the afferent vessels, then in the efferent, and in these last, first in those which, leaving the globule, descend into the tubular substance under the name of straight vessels; lastly the interlobular arteries, and on the other hand, the capillaries may be in turn invaded.

B. Often the vessels alone are affected; however, the walls

of the tubuli may be also affected; and, what is remarkable, it is the inferior extremity of the collecting tubes in the papillary portion, which is in this case the most frequent location of amyloid degeneration; it is only under circumstances relatively rare that the branches of the collecting tubes and convoluted tubes are affected, and as to Henle's loops, it does not appear that they are ever altered.

C. Aside from these lesions of the vessels and of the hyaline membranes, the greatest part of the alterations, otherwise both numerous and profound, presented by the kidney, do not relate to amyloid degeneration. 1st. In the lumen of the tubuli, cylinders are sometimes found which give the reaction upon the use of iodine, but this peculiarity, as we have said, is not absolutely specific. 2d. The epithelium of the tubuli contorti is sometimes degenerated, forming a magma which fills the calibre of the tube, and gives the special reaction, but it is a very exceptional fact. 3d. There may be found, in combination with the amyloid alteration, all the histological traits of parenchymatous nephritis, or rather the characters of a conjunctive interstitial proliferation, and it is to the combination of these various lesions, concomitant with the amyloid alteration, that are due the varied macroscopic appearances that may be presented by the amyloid kidney.

D. Finally, to bring into greater prominence the disposition of the amyloid alteration in the kidney, I consider it useful to study the appearance presented by sections made upon various points of the organ; I will suppose, for example, a case in which the amyloid alteration exists in a high degree, without having invaded, which is not very often the case, however, the epithelial elements.

Upon sections of the *cortical* substance, made perpendicularly to the surface, we find the entire system of glomeruli, the afferent and efferent vessels, and the interlobular arteries modified by the amyloid degeneration, and having the appearance of being injected by a foreign substance.

The sections of the medullary substance are still more in-

teresting. In those made in the region of the papilla we recognize: collecting tubes with thickened walls, and perhaps containing casts; small tubes with thickened walls, striated; these are the vasa recta; finally, small tubes presenting no alteration, and which are no other than Henle's loops.

On sections made in the vicinity of the cortical substance, we find the straight vessels altered, disposed in small groups about lobules and in the intervals limited by them; Henle's loops and the straight tubes present no appreciable lesion.

E. Next in order are the *macroscopic* characters. 1st. In the first degree the kidney in all respects presents the aspects of the normal state, and only the tincture of iodine reveals the alterations of the glomeruli, an alteration as yet quite limited, and which, clinically, is manifest by no appreciable symptom.

2. When the patient succumbs one or two years after the commencement of the disease, the kidney presents the aspect of the large smooth kidney, or of the large fatty kidney; the weight and volume are considerable. The histological examination shows the existence of a hypertrophy of the epithelium with or without the accompaniment of fatty degeneration.

3d. Finally, when death occurs only at the expiration of four or five years, the kidney is found to be small, but pale; the surface then presents a series of depressions and elevations, though never the regular appearance of the granulations of the small red kidney; sometimes cysts are found; in every case the iodine reaction will enable us to distinguish this atrophied amyloid kidney from the contracted kidney of primitive interstitial nephritis, or from the small kidney of parenchymatous nephritis which has reached its last stage.

IV.

It remains, gentlemen, to point out to you (and I will do so in a summary manner) the principal clinical phenomena which aid in the recognition of amyloid degeneration of the kidney. It may be said that there are no symptoms which belong to it specifically. The phenomena associated with it are sometimes those of parenchymatous, and sometimes those of interstitial nephritis; sometimes, finally, the two classes of symptoms are found mingled together. Nothing, however, is easier, generally, than to establish the diagnosis, but this is founded almost exclusively upon extrinsic considerations.

The existence of an habitual albuminuria and the persistence of a certain degree of œdema are sufficient in this case to enable us to recognize that we have to deal with a renal lesion, but only the presence of phenomena belonging to the amyloid diathesis reveals the special nature of the kidney affection. Thus, the patient is phthisical, suffers with prolonged suppuration or syphilitic cachexia. We recognize, besides, the existence of a considerable swelling of the liver and spleen; finally, the patient suffers from unmanageable diarrhœa, of a watery and painless character, proceeding from the amyloid affection of the arteries of the small intestines. When these conditions exist, it is easy to recognize and affirm the existence of amyloid degeneration of the kidney.

For the rest, we have not up to the present time succeeded in recognizing distinctly, how in such a case, the parenchymatous or interstitial alterations of the kidney depend upon the amyloid alteration of the arteries, no more than we have in establishing the physiology of the symptoms which depend upon these alterations. These are questions the solution of which is reserved for the future.

EXPLANATION OF PLATE.

PLATE I.

LARGE WHITE KIDNEY—CONTRACTED KIDNEY.

FIG. 1.—External aspect of the kidney after Plate IV., Fig. 1, of *Reports of Medical Cases*, etc., of R. Bright. The kidney was almost white.

FIG. 2.—External aspect of contracted kidney. Dimensions normal. (This figure was engraved from a drawing from nature by M. Gombault.)

Fig. 1.

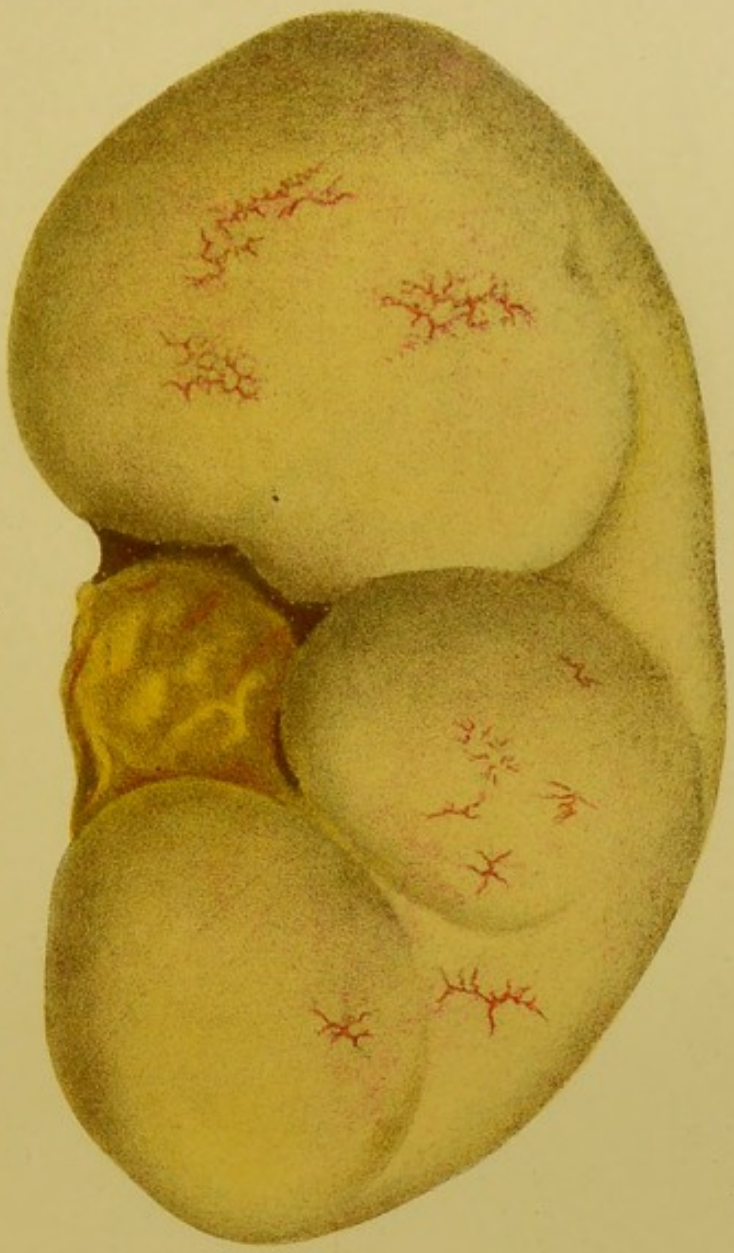

Fig. 2.

A. Karmanski chromo-lith

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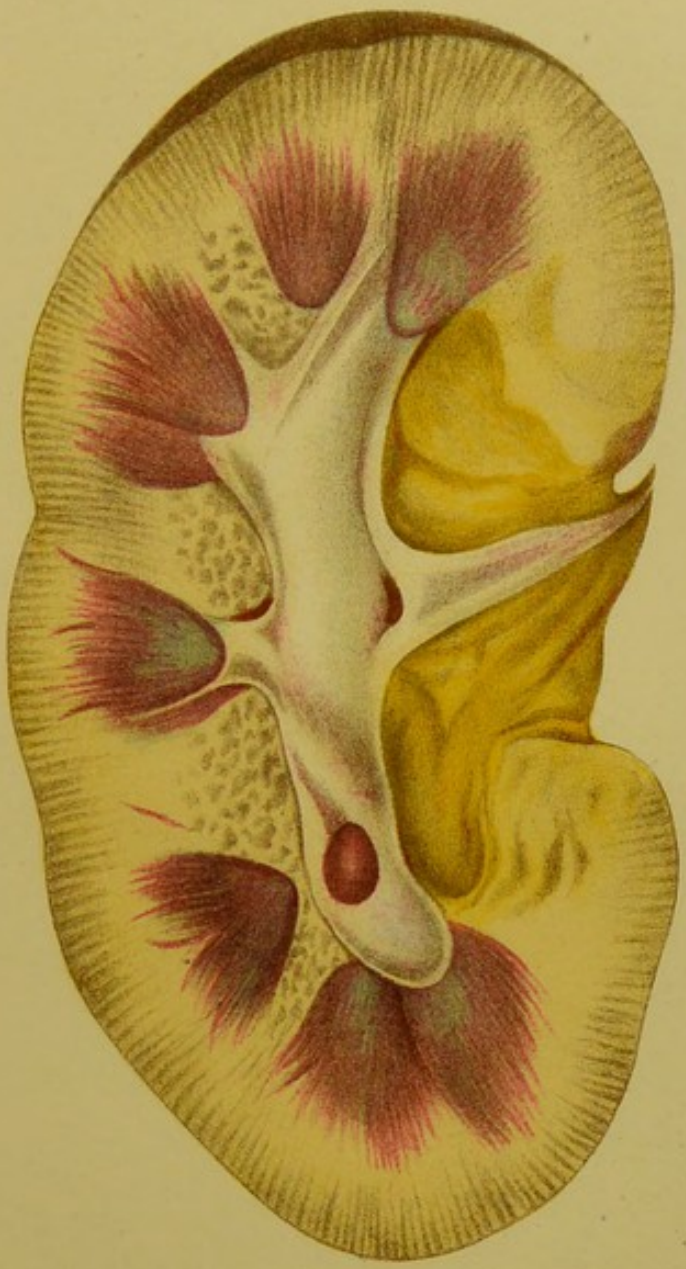
EXPLANATION OF PLATE.

PLATE II.

LARGE WHITE KIDNEY.

Longitudinal section of the kidney represented in Plate I. It shows that the white coloration prevails in the whole of the cortical portion, which admits, however, of its radiated portion being seen. The tubular portion of the kidney had a brilliant color. (R. Bright, *Reports of Medical Cases*, Pl. IV., Fig. 2.)

Fig 3.



A Karmanski chromo lith.

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