This is a digital copy of a book that was preserved for generations on library shelves before it was carefully scanned by Google as part of a project to make the world's books discoverable online.

It has survived long enough for the copyright to expire and the book to enter the public domain. A public domain book is one that was never subject to copyright or whose legal copyright term has expired. Whether a book is in the public domain may vary country to country. Public domain books are our gateways to the past, representing a wealth of history, culture and knowledge that's often difficult to discover.

Marks, notations and other marginalia present in the original volume will appear in this file - a reminder of this book's long journey from the publisher to a library and finally to you.

Usage guidelines

Google is proud to partner with libraries to digitize public domain materials and make them widely accessible. Public domain books belong to the public and we are merely their custodians. Nevertheless, this work is expensive, so in order to keep providing this resource, we have taken steps to prevent abuse by commercial parties, including placing technical restrictions on automated querying.

We also ask that you:

+ *Make non-commercial use of the files* We designed Google Book Search for use by individuals, and we request that you use these files for personal, non-commercial purposes.

+ *Refrain from automated querying* Do not send automated queries of any sort to Google's system: If you are conducting research on machine translation, optical character recognition or other areas where access to a large amount of text is helpful, please contact us. We encourage the use of public domain materials for these purposes and may be able to help.

+ *Maintain attribution* The Google "watermark" you see on each file is essential for informing people about this project and helping them find additional materials through Google Book Search. Please do not remove it.

+ *Keep it legal* Whatever your use, remember that you are responsible for ensuring that what you are doing is legal. Do not assume that just because we believe a book is in the public domain for users in the United States, that the work is also in the public domain for users in other countries. Whether a book is still in copyright varies from country to country, and we can't offer guidance on whether any specific use of any specific book is allowed. Please do not assume that a book's appearance in Google Book Search means it can be used in any manner anywhere in the world. Copyright infringement liability can be quite severe.

About Google Book Search

Google's mission is to organize the world's information and to make it universally accessible and useful. Google Book Search helps readers discover the world's books while helping authors and publishers reach new audiences. You can search through the full text of this book on the web at http://books.google.com/

LANE MEDICAL LIBRARY STANFORD
J53 .H47 1921 STOR
Urinary analysis and diagnosis by micros

LANE
MEDICAL LIBRARY
SEAL OF THE LELAND STANFORD JUNIOR UNIVERSITY
SEMPER VIRENS
1885

URINARY

ANALYSIS AND DIAGNOSIS

BY MICROSCOPICAL AND CHEMICAL EXAMINATION

BY

LOUIS HEITZMANN, M.D.
NEW YORK
FORMERLY PROFESSOR OF PATHOLOGY AND BACTERIOLOGY,
FORDHAM UNIVERSITY SCHOOL OF MEDICINE,
FORDHAM, NEW YORK, N. Y.

Fourth Revised and Enlarged Edition

WITH ONE HUNDRED AND THIRTY-ONE ILLUSTRATIONS, MOSTLY ORIGINAL

NEW YORK
WILLIAM WOOD AND COMPANY
1921

Copyright, 1921
By WILLIAM WOOD & COMPANY

Manufactured in the U. S. A.

LANE LIBRARY

THE MAPLE PRESS YORK PA

47
.21

To the Memory

OF

MY FATHER

CARL HEITZMANN, M.D.

WHOSE LIFE-WORK WAS DEVOTED
TO THE
SCIENCE OF MEDICINE

THIS VOLUME IS AFFECTIONATELY

Dedicated

97172

PREFACE TO THE FOURTH EDITION

In the preparation of the present edition of this work, the general plan of the previous editions has been adhered to. No extensive changes have been found necessary, but the text has been thoroughly revised. New chemical tests, which have proven useful and of practical value, have been added. In the part devoted to microscopical examination some portions have been enlarged, others entirely rewritten, and a few old illustrations have been replaced by new drawings.

As before, the book is intended as a purely practical one, and the first part on the chemical examination makes no claims for completeness. Only those tests are given, which can be used with advantage and without the necessity of a completely equipped chemical laboratory, by the general laboratory worker and by the practitioner, who desires to do his own examinations, or to have a practical knowledge of urinary analysis.

A careful microscopical examination of the urinary sediment is of infinite value to the practicing physician in helping him at arriving at correct diagnoses in many doubtful cases, and is frequently of much greater value than the most painstaking chemical examination. This book aims, both by the text and the illustrations, to be of aid in this important topic of clinical pathology.

The last chapter on the Determination of the Functional Efficiency of the Kidneys has been written for this edition by Dr. Walter T. Dannreuther, to whom the author wishes to express his most grateful appreciation.

LOUIS HEITZMANN.

NEW YORK CITY, *April*, 1921,
38 WEST 90TH STREET.

PREFACE TO THE THIRD EDITION.

Since the appearance of the last edition of this work, many advances have been made in the chemical analysis of urine, while microscopical examination and especially microscopical diagnosis still receive comparatively scant attention in most text-books on this subject. Many years of experience and teaching have shown the author that correct diagnoses by means of microscopical examination of urine can frequently be made in cases where other methods are of little or no practical value.

In the present revision of this work, the aim has again been to increase and improve the first part on chemical examination, and to incorporate in it all the simpler methods and tests which have proven of value as an aid to urinary diagnosis in the hands of different authors. Many new tests have been added, and this part has been considerably enlarged, though it makes no claim for completeness. With few exceptions the more complicated tests, which can only be carried out in completely fitted chemical laboratories have, as before, been omitted.

As in the previous editions, the greatest stress has been laid upon the microscopical examination and especially the microscopical diagnosis. In many cases in which the clinical symptoms, although pointing to an affection of the genito-urinary tract, are vague, and even with the aid of chemical analysis of the urine will not admit of a positive diagnosis, microscopical examination, if carefully conducted, will completely clear up the case. Unfortunately the majority of text-books on this subject still teach that diagnosis cannot be made from a microscopical examination of urine, except in those cases in which casts are present. No stress whatever is laid upon the epithelia found in the urine, since it is claimed that a diagnosis as to their location is impossible. Again, no account is taken of numerous other features constantly seen in pathological conditions of the genito-urinary tract, which are of great value in arriving at correct conclusions as to the condition of the patient.

As regards the epithelia, it is undoubtedly an impossibility to diagnose every single epithelium found in urine, but by far the greatest numbers can be correctly located, and valuable deductions made therefrom. Low magnifying powers, such as are frequently used for urine work, are decidedly useless, and a microscopical diagnosis of the different features seen in urine should never be attempted with a magnifying power of less than 400 or 500 diameters. By studying the epithelial formations with such powers in cases where the clinical diagnosis is plain, as for instance in cases of a simple cystitis or a pyelitis, it will soon be seen that the cellular elements are different in the different conditions. Again, a study of the microscopical features in cases of ureteritis, pyelitis or nephritis from specimens taken by means of the ureteral catheter, so much resorted to at the present day, should soon convince even the most skeptical that a location of the majority of the epithelia is possible. When specimens of prostatic secretion are studied in cases of undoubted prostatitis and spermatocystitis, and urines from the same cases are examined, the conclusion that many epithelia can be correctly located seems inevitable.

No attention whatever is paid in text-books as to the possibility of diagnosing the acuteness or chronicity of a lesion, a suppurative or ulcerative condition, degenerations, and a number of other pathological changes, in all of which the features in the urine are characteristic enough. It is evident that a mere description of the features found in different cases cannot be sufficiently clear, but that illustrations made directly from nature are absolutely essential. The illustrations in this volume have been drawn by the author directly from specimens in his possession. The text in the present edition has been carefully revised and additions made where it was deemed advisable.

In the third part, devoted to microscopical diagnosis, full-page illustrations have been added to elucidate the text, each drawing giving the different features in the case it depicts. This subject is undoubtedly of the greatest practical value, and a careful study of the different formations seen in urine cannot fail to show the importance of urinary diagnosis. Many mooted points in the clinical symptoms can often be cleared up by the microscope in a short space of time, and correct conclusions as to the exact condition of the patient arrived at. If microscopical examinations of urine are carried out more carefully than is generally done, even at the present time, urinalysis is bound to become of far greater benefit to both physician and patient than has so far been the case.

LOUIS HEITZMANN.

CONTENTS

Introductory

CHAPTER I

CHAPTER II

PART FIRST

Chemical Examination

CHAPTER III

General Physical and Chemical Properties (page 13)

CHAPTER IV

Normal Constituents (page 24)

A. Organic (page 24)

CHAPTER VI

Carbohydrates (page 60)

A. Grape Sugar (page 60)

B. Other Carbohydrates (page 69)

CHAPTER VII

Other Abnormal Constituents (page 72)

PART SECOND

MICROSCOPICAL EXAMINATION

CHAPTER VIII

General Considerations (page 85)

CHAPTER IX

Crystalline and Amorphous Sediments (page 93)

I. ACIDS AND SALTS (page 93)

II. OTHER UNORGANIZED SEDIMENTS (page 115)

Urinary Concretions (page 119)

CHAPTER X

Blood-Corpuscles and Pus-Corpuscles (page 121)

I. BLOOD-CORPUSCLES (page 121)

II. Pus-Corpuscles (page 125)

CHAPTER XI

Epithelia (page 131)

CHAPTER XII

Mucus and Connective Tissue (page 149)

I. Mucus (page 149)

II. Connective Tissue (page 151)

CHAPTER XIII

Tubular Casts (page 158)

I. True Casts (page 159)

II. False or Pseudo Casts (page 170)

CHAPTER XIV

Micro-organisms and Animal Parasites (page 173)

I. Micro-organisms, or Fungi (page 173)

II. Animal Parasites, or Entozoa (page 187)

CHAPTER XV

Extraneous Matters (page 193)

PART THREE

Microscopical Urinary Diagnosis

CHAPTER XVI

Diseases of the Kidney and Pelvis of Kidney (page 209)

I. Inflammations of the Kidney and Its Pelvis (page 209)

CHAPTER XVIII

Diseases of the Sexual Organs (page 303)

CHAPTER XIX

DETERMINATION OF THE FUNCTIONAL EFFICIENCY OF THE KIDNEYS (page 329)

APPENDIX (page 341)

LIST OF ILLUSTRATIONS.

URINARY ANALYSIS AND DIAGNOSIS.

INTRODUCTORY.

CHAPTER I.

HISTOLOGY AND SECRETION.

THE kidney is a compound tubular gland, which consists of an outer, cortical, and an inner, medullary or pyramidal, substance; its surface is ensheathed by a dense, fibrous connective-tissue capsule. The main constituents of the kidney are the blood-vessels and the uriniferous tubules; these are held together by a delicate, fibrous connective tissue. In the cortical substance, which contains the Malpighian corpuscles, the tubules are convoluted, while in the medullary substance they run a more nearly straight course.

Each Malpighian corpuscle is composed of a delicate connective-tissue capsule—the capsule of Bowman—and the glomerulus or tuft consisting of a number of convolutions of capillary blood-vessels (see Fig. 1). Both the inner or glomerular and the outer free surface of Bowman's capsule are lined by flat epithelium in the adult. Between the capsule and the glomerulus there is a space, the size of which differs according to the state of secretion. The glomerulus is connected with an afferent and an efferent arterial blood-vessel, the former being the larger of the two, while opposite the site of the blood-vessels the uriniferous tubules originate.

The uriniferous tubules are divided into a number of different segments, which are the following: 1. Proximal convoluted tubule. 2. Narrow tubule. 3. Distal convoluted tubule. 4. Arched or straight collecting tubule. From a confluence of a number of collecting tubules the larger collecting tubules are formed, which in turn unite to form the papillary ducts or tubules of Bellini; these pass through the renal papillæ and empty into the calyces and pelvis of the kidney. The course of the uniferous tubules as well as of the blood-vessels is represented in Fig. 2, a diagram of the kidney.

The proximal convoluted tubule originates from the capsule of Bowman as a slightly narrowed, funnel-shaped neck, and, after repeated convolutions in the cortex, tends downward into the medulla. Here it becomes narrow and represents the descending branch of Henle's loop. After reaching certain depths in the medullary substance, it turns upon itself, producing Henle's loop, and passes again toward the surface as the ascending branch of the narrow tubule or of Henle's loop. It now widens, and, at the most peripheral part of the cortex in which there are

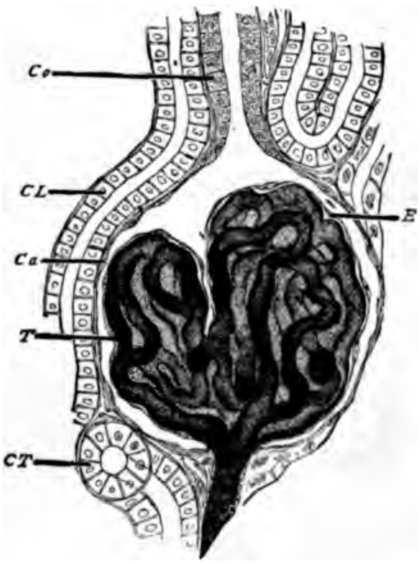

FIG. 1.—MALPIGHIAN CORPUSCLE.

T, Capillary loops of the glomerulus, in connection with the afferent artery, covered by *E*, flat epithelia; *Ca*, capsule covered with flat epithelia, in communication with *Co*, the convoluted tubule; *CL*, convoluted tubule in longitudinal section; *CT*, convoluted tubule in transverse section (× 350).

no glomeruli, again becomes a convoluted tubule—the distal convoluted tubule, also known as the intercalated tubule, which inosculates with the arched or straight collecting tubule. The latter runs down through the medulla, unites with other arched tubules, becomes broader, and enters the papilla as tubule of Bellini, which empties into the calyx and pelvis of the kidney.

The uriniferous tubules are lined by a single layer of epithelia, and each portion has its peculiar epithelial lining. In a general way, this is cuboidal in the convoluted tubules, flat in the narrow, and columnar in the collecting tubules, although different portions of both the narrow and collecting tubules are also lined by cuboidal epithelia. All tubules are

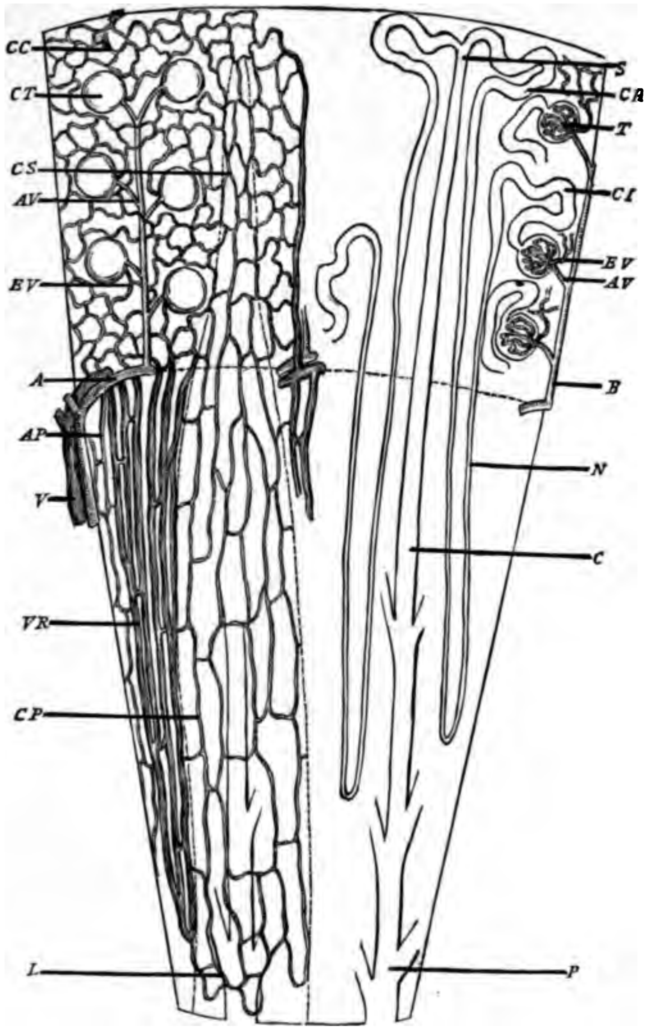

FIG. 2.—DIAGRAM OF THE KIDNEY.

T, Malpighian corpuscle; CT, capsule of Malpighian corpuscle; CI, proximal convoluted tubule; N, narrow or looped tubule; CH, distal convoluted tubule; S, straight collecting tubule in the medullary ray of the cortical substance; C, straight collecting tubule in the medullary substance; P, straight collecting tubule in the papilla; A, renal artery; V, renal vein; AV, afferent vessel; EV, efferent vessel; B, arterial branch to the cortical substance; AP, arterial branch to the medullary substance; CC, capillaries of convoluted tubules; CS, capillaries of narrow tubules; CP, capillaries of straight collecting tubules; VR, blood-vessels of the medullary substance; L, capillaries of papilla. The sum total of the convoluted tubules is termed the labyrinth, while the straight tubules, both narrow and collecting, produce the medullary rays between the labyrinths in the cortex.

surrounded by a delicate connective tissue which carries the blood-vessels and nerves.

The peculiarities of the cortical and medullary substances are shown in Figs. 3 and 4.

FIG. 3.—CORTICAL SUBSTANCE OF THE KIDNEY. TRANSVERSE SECTION. BLOOD-VESSELS INJECTED (× 500).

C, Convoluted tubule; *N*, narrow tubule; *NA*, ascending branch of narrow tubule; *S*, straight collecting tubule.

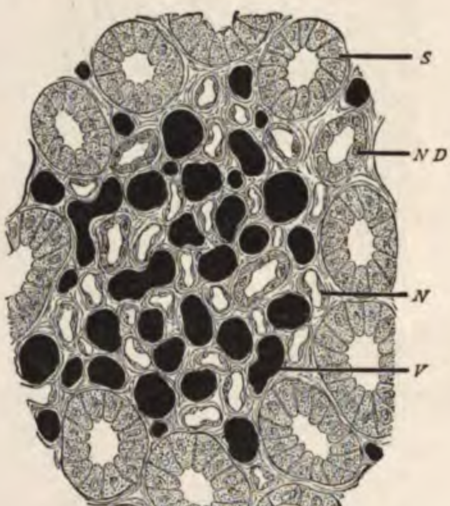

FIG. 4.—MEDULLARY SUBSTANCE OF THE KIDNEY. TRANSVERSE SECTION. BLOOD-VESSELS INJECTED (× 500).

N, Narrow tubule; *ND*, descending branch of narrow tubule; *S*, straight collecting tubule; *V*, blood-vessels.

The vascular supply of the kidney is in intimate relation with the uriniferous tubules. The renal artery divides into a number of branches, known as the interlobar arteries, which, upon reaching the boundary zone between the cortical and medullary substance, bend sharply and produce the arterial arches. Each artery is accompanied by a vein, the

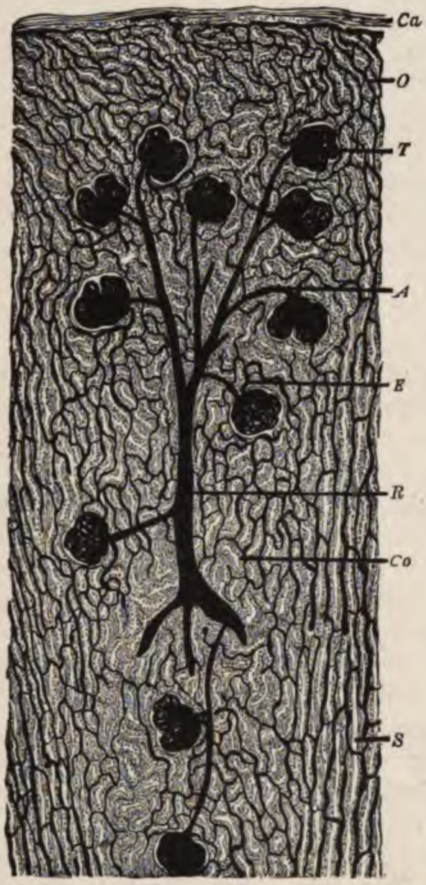

FIG. 5.—INJECTED BLOOD-VESSELS OF THE CORTICAL SUBSTANCE OF THE KIDNEY OF A DOG (× 100).

Ca, Capsule; *O*, outer zone, devoid of Malpighian corpuscles; *T*, Malpighian corpuscle; *A*, afferent vessel; *E*, efferent vessel; *R*, branch of renal artery; *Co*, zone of convoluted tubules; *S*, zone of straight tubules.

veins being connected by lateral branches and producing a venous plexus. From the arches straight arterial branches—the interlobular arteries—arise, which penetrate the cortical substance, divide, and give off numerous transverse twigs—the afferent vessels of the glomerulus (see Fig. 5).

The afferent vessel breaks up into a number of small branches which in turn give rise to groups of capillaries forming the glomerulus. Larger capillaries, arising from the smaller, unite to form the efferent vessel, which leaves the glomerulus near the entrance of the afferent vessel, and is smaller than the latter. The entire blood supply of the glomerulus is arterial. The efferent vessel soon divides freely into capillaries, for the supply of the cortical as well as the medullary substance. In these capillaries the blood gradually becomes venous and passes into the interlobular veins, which accompany the arteries to the boundary between the cortical and the medullary substance; here they enter the venous arches which accompany the arterial arches.

The kidney is richly supplied with medullated and non-medullated nerve fibres, which accompany the arteries and may be traced to the epithelia of the uriniferous tubules.

Urine, the excretion from the kidneys, is produced partly by the process of filtration in the glomeruli, and partly by the activity of the epithelia of the uriniferous tubules. In the glomeruli, not only the water is derived from the blood, but also certain inorganic salts, such as sodium chloride, and possibly a few other solids are separated. The amount of the fluid filtered off depends almost entirely upon the blood pressure in the glomeruli. The epithelia of the uriniferous tubules constitute the true secretory structure of the kidney.

These views, which were first promulgated by Bowman in the year 1842, were later corroborated by experiments of Heidenhain, who injected indigo-carmine into the blood of animals, and found that a blue color appeared in the urine soon afterward, and that the epithelia of the convoluted and ascending branch of the narrow tubules were stained blue, while the Malpighian corpuscles did not show the slightest traces of the stain. After section of the spinal cord, which causes lowering of the blood pressure in the renal glomeruli, and injection of indigo-carmine the epithelia of the uriniferous tubules were stained blue with this substance, which was also found in the lumen of the tubules, while the glomeruli were free from stain. This appears to show that under ordinary circumstances the indigo-carmine is eliminated by the tubular epithelia, and that, when by diminishing the blood pressure the filtration of urine ceases, the substance remains in the tubules.

In the light of our present knowledge upon this subject, it is evident that most of the saline constituents of the urine are the excretory products of those uriniferous tubules which are richly supplied with capillary blood-vessels and the epithelia of which are closely connected with the walls of the vessels. The thickened blood contained in these vessels reabsorbs a portion of the liquid from the tubules and supplies the liquid in the tubules with a certain amount of its salts. The whole process is accomplished through the agency of the living epithelia, and is not to be considered a simple process of osmosis. The differences in the structure of the epithelia in certain portions of the uriniferous tubules, and the striking differences in the distribution of the blood-vessels, strongly point toward a difference in the function of portions of the tubules, even though up to the present time no exact demonstration of these functions concerning the constituent elements of the urine has been furnished.

Pathological conditions also prove that the renal epithelia possess important functions. In diseases in which the function of the tubules is much interfered with, their epithelial lining being destroyed to a considerable degree, urea and allied products are retained in the system, and the phenomena of uræmia result. The urine in such cases is of a more watery character than normally, has a lower specific gravity, and contains a smaller amount of its characteristic solids.

CHAPTER II.

GENERAL REMARKS.

URINARY ANALYSIS, in order to be thorough and of practical value, must necessarily be both chemical and microscopical. Chemical examination, although of great importance, can alone never lead to a correct diagnosis; only through the use of the microscope the nature of the disease in the genito-urinary tract, as well as its exact location, can be revealed. Every urine to be examined should be first subjected to different chemical tests, the extent of which will vary with the different cases, and then to a microscopical examination.

In the majority of cases the simpler chemical tests alone will be required. These must be made, first, with a view of determining the character and amounts of the normal constituents of the urine; secondly, for the purpose of learning of the presence of any abnormal constituent. A general knowledge of the normal constituents is, therefore, necessary; and we must not lose sight of the fact that these may vary to a considerable degree, even in perfect health, partly from diet, and partly from conditions of rest or activity. An increased or diminished amount of any ingredient does not necessarily mean a pathological condition, although when this increase or diminution lasts for a long time a diseased condition becomes certain.

In selecting a specimen for examination, it is essential for accurate diagnosis to obtain the total amount of urine passed during the whole twenty-four hours, or to have the patient collect the entire amount, measure it carefully, note the exact quantity, and send from four to eight ounces of the mixed urine. In collecting the twenty-four hours' amount, mistakes are frequently made. The procedure should be the following: A certain time—for instance, eight o'clock in the morning—is selected for starting the collection of urine; the bladder should be emptied at this time and the urine voided thrown away; every drop of urine subsequently voided is carefully collected, the patient being instructed to void and collect the urine before each movement of the bowels, the last amount taken being at eight o'clock the following morning. The amount of urine is now measured and noted. The urine may be kept in clean bottles of any size, although a bottle holding about half a gallon is preferable.

The reasons for collecting the twenty-four hours' amount are various;

not only is the total quantity voided important in diagnosing different affections, but the proportions of the normal as well as of the pathological ingredients vary considerably at different hours of the day and night, so that the exact amounts of these ingredients cannot be determined when specimens from single urinations are examined. In cases in which the quantitative estimation of urea and solids generally is not essential, or in which the total twenty-four hours' amount cannot be obtained, it is best to obtain the specimen during the day, a few hours after meals, or in the evening. The urine first voided in the morning, although usually the most concentrated, is not the best for examination, since different pathological ingredients, such as albumin and even sugar, may be absent in the morning and yet be present in varying amounts at other times. If any doubt remains as to the exact condition in such cases, two samples, passed at different times, must be tested.

Care should be taken that the bottles in which the urine is kept are scrupulously clean and well corked, and that the urine be obtained in as fresh a condition as possible. When the whole twenty-four hours' urine is collected, the bottle should be kept in a cool place and the urine poured into it as soon as possible after being voided. Even then, secondary changes cannot always be guarded against. In cold weather such changes will usually not take place for many hours, but in warm weather decomposition is apt to set in at the end of a few hours, and bacteria develop in varying numbers. When not absolutely necessary, it is not advisable to add any preservatives to the urine until after the chemical tests have been made. Extraneous objects can easily find their way into the urine when care is not exercised as to cleanliness, and these not infrequently lead to confusion in examination.

When urine is received for examination, it should be set aside for at least six hours, that a sediment may be deposited, unless it is preferred to use the centrifuge, when examination can proceed at once. In the former case the upper part of the urine is used for chemical tests, and the sediment for microscopical examination; while in the latter a small amount is used for the centrifugal apparatus, and chemical examination can at once be conducted with the remainder.

After determining the amount of urine voided in twenty-four hours, we must note the color, odor, transparency, and reaction, and carefully determine the specific gravity. The approximate amount of urea voided in twenty-four hours should then be estimated by chemical tests, and the total amount of solids voided, determined. As urea, the chief organic constituent of urine, forms approximately forty to fifty per cent of all the solid ingredients, the specific gravity of the specimen will frequently give an idea of its increase or diminution in a given case. That errors are liable to result from such an estimation is evident, and wherever possible a ureometer should be used.

The next step should always be the determination of the presence or absence of albumin, as well as its approximate amount if present, while further chemical tests will vary with each individual case. Whenever the specific gravity is above normal, or any clinical symptoms lead to a suspicion of the presence of sugar, even at a low specific gravity, tests for sugar must be resorted to. Should it be desired to know the approximate amounts of uric acid, chlorides, sulphates, and phosphates present, though this is not always essential for the diagnosis, the simpler tests for these ingredients will, as a rule, be all that are required.

Before resorting to microscopical examination, the nature of the sediment, whether it is present in small or large amount, its color, and its general character should be noted; and then all the elements found under the microscope, as well as their comparative numbers, should be carefully observed. It will always be safest to examine a number of drops before coming to a conclusion and determining upon the diagnosis.

PART FIRST.

CHEMICAL EXAMINATION.

PART FIRST.

CHEMICAL EXAMINATION.

CHAPTER III.

GENERAL PHYSICAL AND CHEMICAL PROPERTIES.

Normal urine is a yellowish, transparent liquid, of a peculiar odor, and always of an acid or faintly acid reaction, when the entire twenty-four hours' amount from a person on a mixed diet is tested. This reaction was until recently supposed to be due to the presence of acid salts, especially to acid sodium phosphate (monosodium phosphate or sodium dihydrogen phosphate of the formula NaH_2PO_4), which turns blue litmus paper red, and not to the presence of any free acid. The degree of acidity was believed to depend upon the amount of the acid sodium phosphate as compared with that of the alkaline disodium phosphate (of the formula Na_2HPO_4). Urine is rarely neutral, but it occasionally gives both reactions with litmus paper—that is, turns blue litmus red and red litmus blue. This reaction is known as amphoteric and was supposed to be due to the presence in variable proportions of both acid monosodium and alkaline disodium phosphate.

Recent researches by Folin and others tend to overthrow this theory, and the acidity is now considered to be due to the presence of phosphoric acid, sulphuric acid, and various free organic acids. The different acids which take part in the acid reaction of a urine affect the reaction in proportion to their dissociation, since in accordance with what is known as the "ionic theory," the acid reaction of a solution depends upon the amount of hydrogen ions present.

The degree of acidity of the urine varies at different times of the day, and is considerably influenced by the food. The acidity is, as a rule, highest in the morning before breakfast, and is diminished after a meal on account of the secretion of hydrochloric acid into the stomach. It reaches its lowest point a few hours after a meal, when it may even be temporarily alkaline, and the urine may be turbid from the precipitation of phosphates. This temporary change in the reaction has been called the "alkaline tide" of the urine. An exclusive protein diet causes an increase of acidity, and such an increase is also seen after excessive muscular exercise and after hot baths with free perspiration. After ingestion of large amounts of vegetables and alkaline waters, there is a diminution of acidity, and the reaction may even temporarily become alkaline.

Determination of Reaction.—For all clinical purposes the determination of the reaction by means of litmus paper is sufficient; blue litmus paper turning red in acid urine, and red litmus paper turning blue in alkaline urine. A rough idea of the degree of acidity or alkalinity can be obtained by the intensity of the change in color, and may be noted as "faintly acid or alkaline," "moderately acid or alkaline," and "highly acid or alkaline." When it gives both reactions with litmus paper, as is not rarely the case, the reaction is known as "amphoteric."

For the determination of the total acidity of the urine the most reliable method is that of *Folin:* Place 25 c.c. of urine into a 200 c.c. Erlenmeyer flask, add one or two drops of a five-tenths or one per cent alcoholic solution of phenolphthalein, and 15 to 20 grams of finely powdered potassium oxalate. Shake the mixture thoroughly for one to two minutes and titrate it immediately with a decinormal sodium hydroxide solution, the shaking being continued. The sodium hydroxide is added until a faint but distinct pink color appears and remains permanent; this is the end point. The percentage of total acidity is expressed in terms of the numbers of cubic centimetres of decinormal sodium hydroxide used to neutralize the acidity of the total amount of urine passed in twenty-four hours. The acidity may also be expressed as grams of hydrochloric acid, 1 c.c. of a decinormal sodium hydroxide solution being equivalent to 0.00365 grams of hydrochloric acid. To calculate the acidity of the urine in terms of hydrochloric acid, multiply the numbers of cubic centimetres of decinormal sodium hydroxide required by the twenty-four hour urine by 0.00365. Normally the acidity of the twenty-four hour urine corresponds to between 1.15 and 2.3 grams of hydrochloric acid.

The color of normal urine is yellowish or amber, although the tints even in health may vary considerably and generally depend upon the degree of concentration and the pigments. The reaction also has an influence upon the color, and highly acid urine frequently becomes darker upon standing, due to the oxidation of chromogens.

According to Vogel, the following color tints may be distinguished:

1. Pale yellow 2. Light yellow 3. Yellow	Yellow urines
4. Reddish-yellow 5. Yellowish-red 6. Red	Reddish urines
7. Brownish-red 8. Reddish-brown 9. Brownish-black	Brown or dark urines

Pale or light yellow urines are rarely highly acid, but usually faintly acid, amphoteric, or alkaline, and denote dilution and an increase in the amount of urine. Reddish-yellow to brownish-red urines are usually rich in solid constituents, contain considerable urea, and are not highly acid. Abnormally dark urines may be due to accidental pigments or medicines. A dark yellow or reddish-yellow color may be due to rhubarb, senna, santonin, or considerable salicylic acid; a red color, to antipyrin, antifebrin, sulfonal, or trional; a brownish-black color, to resorcin, tannin, carbolic acid, guaiacol, or thymol; a greenish-black color, to salol or pyrogallol; and a blue or greenish-blue color, to methylene blue.

The average amount of urine passed by a healthy adult in twenty-four hours is about 1,500 cubic centimetres, or 50 ounces, although it varies between 1,200 and 1,800 c.c., women passing somewhat smaller quantites than men. The specific gravity varies from 1.015 to 1.025, the average being 1.020.

The amount of urine voided is greatly influenced by different factors. It is greater the more liquid is taken into the body, and as the amount of solids, which determines the specific gravity, usually remains about the same in health, it follows that the specific gravity will be lower the greater the quantity voided. The amount of the perspiratory excretion has a great bearing upon the quantity of the urine, and in cold weather, when the perspiration is lessened, the urine increases in amount. Different articles of diet, such as tea and coffee, undoubtedly stimulate the excretion of urine. Nervous excitement, anxiety, and hard mental work have the same effect. Bodily exercise, increasing perspiration, lessens the amount of urine, and therefore renders it more concentrated. The specific gravity of urine voided at different hours of the day may, therefore, vary to a great degree, sometimes being as low as 1.002 or 1.003, and at other times 1.030, without indicating, in any manner, a pathological condition.

Consistency and Odor.—Normal urine is of a watery consistency and foams if shaken, though the foam soon disappears when at rest. It has a peculiar, characteristic odor, which is more or less pronounced according to the degree of concentration, and is spoken of as aromatic or urinous. This odor is probably due to the presence of minute quantities of volatile acids, phenylic, taurylic, damaluric and damalic acids. If the urine has become alkaline, it acquires a disagreeable, repulsive, so-called ammoniacal odor, which is due to the presence of bacterial decomposition products (probably ammonia and phenols). When decomposition is pronounced, the odor is liable to become putrid. After ingestion of certain articles of diet and after taking different medicines, the urine emits a more or less characteristic odor. The peculiar odor after eating asparagus is said to be due to methylmercaptan. After the administration of oil of turpentine an odor not unlike violets is produced. The odor of copaiba, cubebs, and oil of sandalwood is communicated to the urine when these drugs are taken internally. An odor, at first not unlike sweet-brier, but soon becoming very offensive, is present when the urine contains cystin.

The solid constituents of normal urine are partly inorganic and partly organic. The total amount of solids voided with the urine in twenty-four hours is between 60 and 70 gm. The following table of Hammarsten gives the average amounts of solids voided by a healthy adult:

1. *Inorganic constituents*	less than	27.0	gm.
Hydrochloric acid, HCl	about	9.35*	
Sulphuric acid, H_2SO_4		2.50	
Phosphoric acid, P_2O_5		2.50	
Nitric acid, HNO_3	less than	0.10	
Sodium oxide, Na_2O		7.90†	
Potassium oxide, K_2O		3.00	
Ammonia, NH_3		0.70	
Calcium oxide, CaO		0.30	
Magnesium oxide, MgO		0.50	
Iron, Fe	less than	0.01	
2. *Organic constituents*		35.0	gm.
Urea	about	30.0	
Uric acid		0.7	
Creatinin		1.0	
Hippuric acid		0.7	
Other organic constituents	a total of	2.6	

These consist of purin bodies, oxalic, oxaluric, lactic, carbamic, and succinic acids, carbohydrates, glycerophosphoric acid, ethereal sulphates of phenol, cresol, pyrocatechin, indoxyl and skatoxyl,

* As sodium chloride, 15 gm. † As sodium chloride, 15 gm.

pigments, chromogens, ferments, and a few other non-important substances.

The constituents vary considerably under normal conditions, and according to Parkes the composition of normal urine is as follows:

AMOUNTS OF URINARY CONSTITUENTS ELIMINATED IN TWENTY-FOUR HOURS.

Constituents	Average man, weight 66 kilograms. Grams	Per kilogram of body-weight. Grams
Water	1500.00	23.000
Total solids	72.00	1.100
Urea	33.18	0.500
Uric acid	0.55	0.008
Hippuric acid	0.40	0.006
Creatinin	0.91	0.014
Pigments and other organic substances	10.00	0.151
Sulphuric acid	2.01	0.030
Phosphoric acid	3.16	0.048
Chlorin	7–8.00	0.126
Ammonia	0.77	
Potassium	2.50	
Sodium	11.09	
Calcium	0.26	
Magnesium	0.21	

The urinary pigments or coloring matters found in urine are urochrome, which gives the yellow color to the urine; hæmatoporphyrin, urohæmatin, uroerythrin, uroindican, and urobilin. The latter is not, as a rule, found in freshly voided urine, but is always found after standing; hence it is present as a chromogen, named urobilinogen. All of these coloring matters are not necessarily present in every urine, the three important ones being urochrome, hæmatoporphyrin, and urobilin.

The gaseous constituents are carbonic acid, nitrogen, and oxygen, the latter in very small amount only.

Transparency and Changes upon Standing.—Normal, freshly voided urine is always perfectly clear, but if left at rest for a few hours a cloudy sediment, more or less pronounced, forms, and is usually more marked in the urine of females. This sediment, which at first usually floats in the centre of the urine and gradually settles at the bottom, is known as *nubecula*, and disappears entirely upon shaking. It consists of mucus, with a few flat epithelia from the bladder, and, in the urine of females, from the vagina. In addition to these features, epidermal scales from the prepuce and nymphæ will always be found, and spermatozoa may also be present. At the time of menstruation the urine is red and contains numerous red blood corpuscles. A normal acid urine may, after a few hours, precipitate some amorphous urates, then a few uric-acid crystals, and occasionally a small number of calcium-oxalate crystals.

After the urine has remained standing for one or more days, bacteria develop, their number and rapidity of development depending upon the temperature. In warm weather they may appear in the course of a few hours. In highly acid urine conidia and mycelia not infrequently form, though cocci and bacilli may also be found. Saccharomycetes or yeast fungi may similarly develop in acid urine; these are most commonly, though not exclusively, seen in urine containing sugar. In alkaline urine fission fungi—both cocci and bacilli—are seen in large numbers. When ammoniacal decomposition of the urine sets in, the urea is gradually transformed into ammonium carbonate through the activity of the micro-organisms. Such a urine becomes turbid or opaque from the presence of the fission fungi and precipitated phosphates. The deposit of amorphous urates now becomes transformed into ammonium urate, while uric-acid and calcium-oxalate crystals disappear, and characteristic crystals of triple phosphates develop.

Under Pathological Conditions the urine may be passed as a cloudy liquid of varying consistency. The highest degree of viscidity is usually found in chronic cystitis, when the urine, being strongly alkaline and decomposing in the bladder, appears as a viscid, stringy, muco-purulent mass, with a repulsive ammoniacal odor; it contains a varying number of bacteria and a large amount of phosphates. In suppurative conditions the urine often has a peculiarly offensive, putrid odor. In severe cases of diabetes a sweet or fruity odor of acetone is often imparted to the urine, while a fecal odor is present in cases of fistula communicating with the intestines.

The color of the urine will be greatly changed by an increase or decrease of the normal coloring matters or the abnormal presence of biliary matter. Biliary pigments color the urine reddish-brown, brown, or greenish, and give to it a greenish-yellow foam. When the urine is mixed with blood it will be more or less dark colored. In febrile conditions it is, as a rule, highly acid in reaction, and has a reddish or reddish-brown color, partly due to an excessive amount of urates, and partly to the presence of uroerythrin. The same may be the case in many slight disturbances of the system. In the rare cases of chyluria the urine is milky in character.

The following table modified from Halliburton shows the nature and origin of the chief variations in the color of the urine:

Color	Cause of coloration	Pathological condition
Nearly colorless.........	Dilution or diminution of normal pigments	Nervous conditions, hydruria, diabetes insipidus, chronic interstitial nephritis, anemia, chlorosis
Light or straw yellow....	Polyuria	Diabetes mellitus
Highly colored..........	Concentration, uroerythrin	Acute fevers, inflammations, hyperæmia of kidneys
Milky...............	Pus corpuscles	Purulent diseases of the genito-urinary tract
	Fat globules	Chyluria
Orange.................	Excreted drugs, santonin, chrysophanic acid.	
Red or reddish.......	Hæmatoporphyrin, unchanged hæmoglobin, pigments in food (logwood, madder, bilberries, fuchsin), antipyrin, sulfonal, trional, antifebrin	Hæmorrhages or hæmoglobinuria
Dark, smoky............	Salol, guiacol, tannin, resorcin, alkapton	Alkaptonuria
Brown to brown-black.	Hæmatin	Small hæmorrhages
	Methæmoglobin	Methæmoglobinuria
	Melanin	Melanotic sarcoma
Greenish-yellow, greenish-brown, approaching black	Bile pigments, pyrogallic acid	Icterus
Dirty green or blue...	Methylene blue A dark blue scum on surface with a blue deposit, due to an excess of indigo-forming substances	Cholera, typhus; seen especially when the urine is putrefying
Brown-yellow to red-brown, becoming blood-red upon addition of alkalies	Substances introduced into the system, contained in senna, rhubarb and chelidonium	

The sediment may be considerably increased. An increased amount of uric acid gives a red, so-called brick-dust sediment, which also adheres to the sides of the vessel, while an excess of amorphous urates gives a heavy, turbid, so-called clay-water sediment. The presence of inflammatory products, phosphates, or bacteria may produce a flaky or granular sediment, and the presence of filaments or threads from the urethra or prostate gland in cases of urethritis and prostatitis a flocculent sediment. A ropy sediment is present in cases of chronic cystitis when the urine decomposes in the bladder, and a purulent sediment in suppurative conditions of the genito-urinary tract.

The amount of urine varies considerably, in many pathological conditions. Increased quantity of urine is known as *polyuria*, diminished quantity as *oliguria*, partial or complete suppression as *anuria*. Polyuria must be distinguished from *pollakiuria*, which signifies frequent urination without regard of the quantity of urine voided. The excretion of an increased amount of urine with normal or reduced total solids for twenty-four hours is known as *hydruria*. The urine is increased in amount in most cases of diabetes mellitus, and its specific gravity is generally high—1.030, 1.040, or more—although the color is frequently pale, even straw yellow. In some cases of diabetes, however, the specific gravity may not only be normal, but below normal—1.015, 1.012, or less—and still a large amount of sugar may be present. The quantity of urine is also considerably increased in diabetes insipidus, in hysteria, convulsions, convalescence from different acute inflammatory diseases, hypertrophy of the heart, and chronic nephritis, especially cirrhosis of the kidney. Patients suffering with cirrhosis constantly void large quantities of pale, at times colorless urine, with greatly decreased solid constituents and a specific gravity frequently below 1.010.

The amount of urine is decreased in acute inflammations of the kidney, as well as in acute inflammatory conditions of the other organs and acute fevers. The urine may be more or less completely suppressed in uræmia, in the last stages of cholera and yellow fever, in rapidly progressive forms of anæmia, in shock due to internal injuries, after catheterization, and in obstructive diseases of the urinary passages. In persons suffering from nephritis it may be suppressed after the administration of anæsthetics.

Determination of Specific Gravity.—The simplest method of ascertaining the specific gravity is by means of the urinary hydrometer or urinometer (see Fig. 6), which, if carefully constructed, will be sufficiently accurate for all practical purposes. If tested with distilled water, such a urinometer will sink to the 1.000 mark at the average temperature of the room. The specific gravity of a specimen should be taken only after it is cooled; otherwise errors will result. The glass cylinder supplied with the instrument should be fluted, so that the latter will not cling to the side of the glass. The test is made as follows: Fill the cylinder four-fifths full of urine, removing the froth, if any is present, with filtering paper. Place the urinometer in the urine, being careful not to allow it to come in contact with the walls of the vessel. Bring the eye on a level with the surface of the urine, and read the corresponding division of the urinometer, but not the upper rim of the fluid, raised a little by capillary attraction. Touch the stem, causing the urinometer to sink slightly in the fluid, and, after it has come to rest, read again.

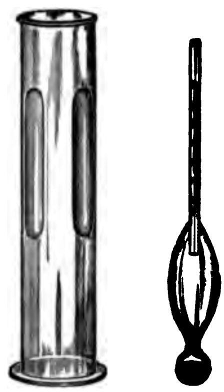

FIG. 6.—URINOMETER.

If the amount of urine is small, dilute the specimen with one, two, or even three volumes of water; test as before directed, and multiply the number of the division mark by the number of volumes used in the process of dilution. For example, if two volumes of water have been added to one volume of urine, thus making three volumes in all, and the urinometer stands at 1.006, the real specific gravity of the original urine is 1.018. The solid materials upon which the specific gravity depends, which were dissolved in one volume, are, after dilution, dissolved in three volumes, and the specific gravity is therefore only one-third of the original.

As indicated above, the temperature is important, and the specific gravity should never be taken when the urine is freshly voided. The urinometers are graduated at a temperature of about 15.5° to 17.5° C. (60° to 63.5° F.). If the urine is warmer than this temperature, one-third of a urinometer degree should be added for each degree of urine temperature; if colder, one-third of a urinometer degree should be subtracted for each degree of urine temperature. A temperature scale is found on many urinometers, or a thermometer is supplied with the instrument.*

More accurate methods for determining the specific gravity are the pyknometer and the Mohr-Westphal balance. The latter is useful only in most exact work. With the pyknometer exact estimations can also be obtained. The principle of this method depends upon the determination of the weight of a definite volume of urine as com-

* Squibb's urinometers, which are used considerably in this country, are standardized at 25° C. or 77° F., a more convenient temperature for clinical work.

pared with that of the same volume of distilled water at exactly the same temperature, the specific gravity being deduced from the ratio of these two weights. Neither of these two methods is sufficiently simple for general practical work.

For the estimation of the specific gravity in the smallest amounts of urine, *Saxe* has devised a special form of hydrometer, which he calls the urinopyknometer. This hydrometer determines the specific gravity of about 3 c.c. of urine, and where small quantities of urine only are available, as in infants or after catheterization of the ureters, it is of considerable value and of a fair degree of accuracy.

Saxe's urinopyknometer (see Fig. 7) consists of a small flask with a well-fitting glass stopper, the head of which bears a tiny bead of mercury. The flask is attached to a small spherical bulb, over which is the stem of the instrument, graduated in reverse order as compared to the ordinary urinometer—that is the mark 1,060 is at the top of the stem and the mark 1,000 at the bottom. When the flask is filled with distilled water up to the mark, and when the instrument is closed and immersed in a glass cylinder filled with distilled water, it reads 1,000 at the level of the distilled water. When urine is poured into the flask to the same mark, the instrument sinks in distilled water in proportion to the specific gravity of that urine, which is then read on the scale. The same precautions in reading must be taken as with the urinometer, and the flask must be perfectly clean and dry. The urine must be poured in accurately with a small dropper until it reaches the mark, so that the lower meniscus touches it as the flask is held at the level of the eye.

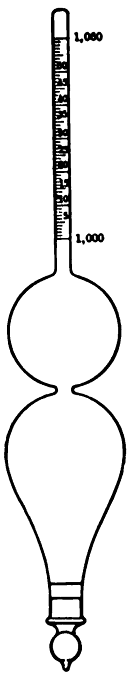

FIG. 7.—SAXE'S URINOPYKNOMETER.

Determination of Solids.—To determine the amount of solids present in the urine voided during twenty-four hours, for practical work, the exact quantity passed during this time, as well as its specific gravity, must be known. The specific gravity is directly dependent upon the amount of solids in solution, a diminution of the solids giving a lower, an increase a higher, specific gravity.

For clinical purposes the amount of total solids voided can be approximately determined by multiplying the last two figures of the specific gravity by the coefficient of Haeser, which is 2.33; this gives the number of grams of solid matter in 1,000 c.c. of urine. This number, multiplied by the number of cubic centimetres passed in twenty-four hours and divided by 1,000, will give the amount of solid constituents eliminated during that time.

Suppose, for example, 1,500 c.c. of urine were passed in twenty-four hours, of a specific gravity of 1.020. To estimate the amount of solids, multiply the last two figures, 20, by the coefficient, 2.33, and by 1,500, and divide by 1,000, thus:

$$\frac{20 \times 2.33 \times 1{,}500}{1{,}000} = 69.90 \text{ gm.}$$

Or, $20 \times 2.33 \times 1.5 = 69.90$. Again, if 1,250 c.c. of urine were passed, of a specific gravity of 1.018: $18 \times 2.33 \times 1.25 = 52.425$ gm., the total amount of solids voided in twenty-four hours.

Valuable conclusions as to the amount of solids may thus be obtained from the specific gravity in a very short time. In diabetes, for instance, the quantity of urine voided being large and of a high specific gravity, the amount of solids is considerably increased; in inflammations of the kidney, on the other hand, where the quantity of urine is decreased and the specific gravity is low, the amount of solids is diminished. No deductions, however, can be drawn from the amount of total solids as to the amount of any particular solid, especially urea. Although urea constitutes from forty to fifty per cent of all the solids excreted in healthy individuals, in pathological conditions the proportions of urea and the other solid constituents often vary to a considerable degree.

The coefficient of Haeser was calculated on the basis of the specific gravity determined at a temperature of 15° C., and, although in universal use, is claimed to be inaccurate for conditions existing in America. Long therefore uses the coefficient 2.6, which was determined for urine the specific gravity of which was taken at a temperature of 25° C. To determine the approximate number of grains of solids in each fluidounce of urine, multiply the last two figures of the specific gravity by Haines' coefficient, which is 1.1. When this figure is multiplied by the total number of ounces voided during twenty-four hours, the excretion of total solids in grains is obtained.

CHAPTER IV.

NORMAL CONSTITUENTS.

A. ORGANIC.

Total Nitrogen.—The total output of urinary nitrogen is the best index of the metabolism of the proteins. This output depends upon the amount of nitrogen taken into the body with the food, as well as upon the degree of tissue metabolism. Normally the proportion between the intake and the output of nitrogen is equal, so that a healthy person is in a condition of nitrogenous equilibrium. Of the total nitrogen eliminated from the body between ninety-three and ninety-five per cent is excreted in the urine and the remaining five to seven per cent in the fæces. Minute amounts escaping from the skin and the lungs can be neglected.

The normal amount of total nitrogen in the urine of a person upon a mixed diet varies between 10 and 16 gm. (150 to 250 grains) in twenty-four hours. The total nitrogen output is increased as a result of increased protein metabolism. The amount is greater after a heavy protein diet, reaching its maximum a few hours after such a meal, also after exercise on account of increased muscular activity, after hot baths, and after drinking considerable quantities of water, since with an increase of water excretion that of nitrogen is also increased. The total nitrogen output is diminished on a low nitrogen diet, and also on one rich in carbohydrates and fat; when the water excretion is reduced on account of sweating; during pregnancy, and after the administration of certain drugs, especially quinine and opium.

Pathologically the nitrogen output is especially increased in acute febrile infections, but also in cachectic conditions in which there is a rapid waste of tissues; in diabetes mellitus and insipidus; in all conditions in which a diminished absorption of oxygen occurs, such as dyspnœa and severe hæmorrhage; after various poisons such as phosphorus, arsenic, antimony and other metallic poisons; finally during the absorption of an exudate or a transudate. It is diminished in convalescence from acute and chronic diseases; in conditions of depressed vitality, as well as in all conditions in which the absorption of the proteins is interfered with. During the formation of an exudate or a transudate, or whenever the water output is diminished the nitrogen is diminished; also in cases of nephritis due to a renal insufficiency and to the associated œdema; finally just before death from any cause.

The nitrogenous constituents of the urine are urea, ammonia, uric acid, purin bases, creatinin, and the so-called "undetermined nitrogen." The latter is made up of different substances present in variable, though small amounts; it includes hippuric acid, the amino-acids, oxy-proteic and alloxy-proteic acids, and allantoin. The distribution of these various nitrogenous products, called the "Nitrogen partition of the urine," varies according to the diet. This distribution among urea and the other nitrogenous constituents depends, according to Folin and others, upon the absolute amount of the total nitrogen excreted. It was found that a decrease in the total nitrogen excretion was always accompanied by a decrease in the percentage of urea. While in persons upon a mixed diet between eighty and ninety per cent of the total nitrogen excreted is urea, upon a nitrogen-free diet no more than sixty to sixty-five per cent appears in the urine as urea. This reduction in the uea excretion upon a nitrogen-free diet is made up by an increase in the other factors, especially the ammonia and creatinin, both of which are relatively increased by percentages, although they may be absolutely diminished. According to the same authors, urea is the only one of the nitrogenous excretions which is both relatively and absolutely diminished as a result of decreased protein metabolism. Cases have been reported in which less than twenty per cent of the total nitrogen appeared in the urine as urea.

Considerable clinical value has also been placed upon the nitrogen partition in pregnancy, in which there is normally in many cases a disturbance of metabolism, diminishing the urea and increasing the ammonia and the undetermined nitrogen. The amount of the latter is claimed to be especially high when toxic symptoms of any kind develop during pregnancy, so that in all such cases a careful determination of the different nitrogenous ingredients of the urine may be helpful to the clinician.

The method used for the estimation of total nitrogen is that of Kjeldahl, which, however, is too complicated for ordinary clinical work, so that the clinician usually relies upon the estimation of urea, ammonia and uric acid. Kjeldahl's method is based upon the fact that the nitrogenous constituents of the urine, when heated with concentrated sulphuric acid, are oxidized to ammonium sulphate. The latter is then decomposed by means of a caustic alkali and distillation, and the gaseous ammonia thus given off is collected in a known quantity of standard solution of an acid. The solution is then titrated with a standard alkali, and the difference between the acidity thus shown and its original acidity furnishes an index of the ammonia absorbed, and consequently of the total nitrogen. Every cubic centimetre of tenth normal sulphuric acid, used by the ammonia liberated in the distillation, represents 0.001401 gm. of nitrogen.

Urea.—Urea or carbamide (CON_2H_4) is the chief organic constituent of urine and the most important nitrogenous waste product found in urine. The greater portion of nitrogen taken into the system as food is excreted by the kidneys in the form of urea, which substance represents between eighty and ninety per cent of the total nitrogen of the urine, with the person upon a mixed diet; upon a nitrogen-free diet it represents only between sixty and sixty-five per cent. The amount of urea excreted varies greatly under different physiological conditions, ranging between 20 and 35 or 40 gm., or approximately between 310 and 620 grains in twenty-four hours; this represents from forty to fifty per cent or more of all the solid ingredients voided. As urea is the most abundant solid of urine, it influences the specific gravity most, which latter will therefore give an approximate idea of an increase or decrease of urea. A specimen of normal urine, with a specific gravity of 1.020 and voided in a quantity of about fifty ounces (1,500 c.c.), will contain about 450 or 500 grains of urea (28 to 31 gm.), or 9 to 10 grains to the ounce, or about two per cent.

Normally the amount of urea excreted varies greatly with the diet; it is most abundant after an exclusive meat diet, less abundant after a mixed, and least abundant after a strictly vegetable diet. It is increased after muscular exercise and mental activity. Pathologically it is increased in acute fevers, owing to increased tissue metabolism, and in diabetes, in the latter condition sometimes to a considerable degree. It is decreased in diseases of the liver—the liver being the chief seat of the formation of urea—in diseases of the kidney, and in chronic affections impairing the vitality of the patient.

Urea is frequently decreased in normal pregnancy. It is a common and undoubtedly commendable practice to examine the urine for urea at stated intervals during pregnancy. Unfortunately, the many different factors which should be taken into account, such as diet, exercise, and the condition of the gastro-intestinal tract, are frequently overlooked, and unnecessary anxiety is caused by a continued diminution in the amount of urea excreted. In these cases too much significance should not be attached to the decreased amount of urea alone, but all the important chemical tests, as well as thorough microscopical examination, must be resorted to before alarming the patient or her relatives.

FIG. 8.—CRYSTALS OF UREA (UPPER HALF) AND NITRATE OF UREA (LOWER HALF) (× 200).

Urea is always held in solution and can never be found under the microscope without chemical means. It crystallizes in the form of colorless quadrilateral plates or prisms, and in needles of varying sizes. It is readily soluble in water and alcohol, but is insoluble in ether. Urea can easily be detected as nitrate of urea by placing a few drops of urine upon a glass slide, adding a drop of nitric acid, warming the slide carefully, and placing it aside to crystallize. Under the microscope more or less regular rhombic or hexagonal plates, either single or overlapping each other, may now be found. These plates have a little color and are perfectly characteristic (see Fig. 8). With oxalic acid it forms oxalate of urea, in the form of flat or prismatic crystals.

Quantitative Tests.—The quantitative tests for determining the exact amount of urea present in the urine are numerous, but more or less complicated. The clinically available methods are by no means accurate, but sufficiently so for general practical work. The most inaccurate is the approximate estimation of urea by means of the specific gravity. As urea is the most abundant solid constituent of the urine, it influences the specific gravity most, which latter runs closely parallel to the amount of urea, provided that the chlorides are normal, no sugar is present, and the urine contains no albumin, or a small amount only. In such cases the percentage of urea practically parallels the last two figures of the specific gravity; a specific gravity of 1,020, for instance, conforms with the presence of 2 per cent of urea; one of 1,018 with 1.8 per cent; of 1,024 with 2.4 per cent; and of 1,009 with 0.9 per cent. The variations in the majority of such cases are rarely more than 0.1 per cent in either direction. Such rough estimations should, however, never be made where the entire twenty-four hours' urine is available, but can be made with single voidings, since neither the specific gravity nor the amount of urea of a single voiding, or even that of the night and morning urine combined can give any idea of the correct readings for twenty-four hours. An increase or diminution in the amount of the chlorides present, however, materially influences the specific gravity.

Hypobromite Method.—The best and simplest of the clinically available methods is the hypobromite method, introduced by Knop, the principle of which depends upon the fact that, when urea comes in contact with an alkaline sodium-hypobromite solution, it is decomposed into nitrogen, carbon dioxide, and water, according to the following equation:

$$CO(NH_2)_2 + 3NaBrO = 3NaBr + 2H_2O + CO_2 + N_2.$$

The carbon dioxide which develops is absorbed by the sodium hydroxide, while from the volume of nitrogen liberated the amount of urea can be calculated.

The quickest way of carrying out this method is by means of Doremus' ureometer. The hypobromite solution necessary for this test does not keep well, and it is therefore best to keep the bromine and the caustic-soda solution separate. Have on hand a solution of sodium hydroxide—100 gm. of caustic soda to 250 c.c. of water (or four ounces to ten of water)—and the bromine, in separate bottles. To prepare the solution for immediate use, take 10 c.c. of the sodium hydroxide solution and add 1 c.c. of bromine; mix thoroughly, dilute with 11, 12, 13 or 14 c.c. of water, and the solution is then ready for use. A glass graduate, of a capacity of 25 c.c., will be found the most convenient for this purpose.

Instead of using pure bromine, which is disagreeable to handle, Rice's solutions may be substituted and give good results. The

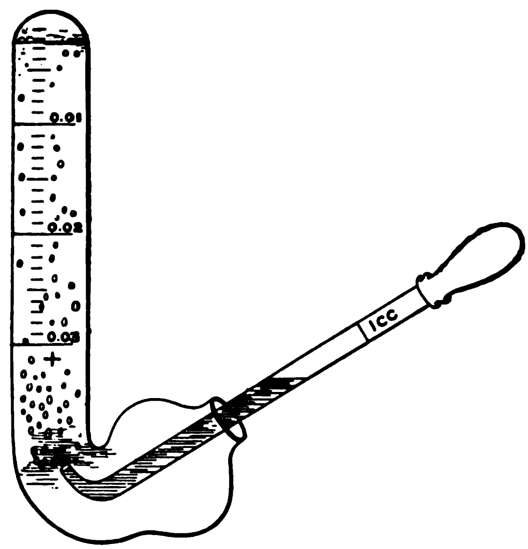

FIG. 9.—DOREMUS' UREOMETER.

bromine is replaced by a solution composed of one part each of bromine and potassium bromide and eight parts of water. The two solutions to be kept separately are (1) caustic soda, 100 gm., distilled water, 250 c.c.; (2) bromine, 30 c.c., potassium bromide, 30 c.c., distilled water, 240 c.c.; these solutions keep indefinitely. For immediate use, take 5 c.c. of each of these solutions, mix, and dilute with 10, 12 or 14 c.c. of water. In both cases fill the bulb of the ureometer with the solution and proceed as stated below.

Doremus' apparatus (see Fig. 9) consists of a bulb and graduated tube and a small curved nipple-pipette to hold 1 c.c. of urine. The bulb of the ureometer is filled with the hypobromite solution, and by inclining the tube the long arm is filled to the bend in the bulb. By means of the nipple-pipette 1 c.c. of urine is drawn up, the pipette passed through the bulb of the ureometer as far as it will go in the bend, and the nipple compressed gently and steadily. The urea instantly decomposes, and the bubbles of nitrogen rise in the long arm of the instrument, while the displaced liquid flows into the bulb. The decomposition of urea is complete in from five to twenty minutes, and the graduation on the tube indicates the quantity of urea in 1 c.c. of urine. Two forms of the instrument are furnished—one graduated to read fractions of a gram to the cubic centimetre of urine, the range being from 0.01 to 0.03 gm.; to obtain the percentage, multiply the number of divisions on the tube by 100; thus, 0.02 gm. to the cubic centimetre is two per cent of urea. The other form of the instrument is graduated to show the number of grains of urea per fluidounce of urine.


FIG. 10.—HINDS' MODIFICATION OF DOREMUS' UREOMETER.

Hinds' modification of the Doremus apparatus (see Fig. 10) is more convenient and more accurate than the original form, as it obviates the use of a pipette. The amount of urine is measured more exactly, being introduced into the graduated small tube and the flow controlled by the stopcock.

In using the Doremus' ureometer, the urine should theoretically be free from both albumin and sugar. Practically, however, these substances need not be removed, since the method never yields accurate results. When more than a trace of albumin is present in the urine, a dense froth collects in the ureometer tube while the urine is injected; this froth forms first in the upper portion of the tube, but, when the amount of albumin is large, soon becomes disseminated throughout the entire tube. It settles slowly, so that frequently the percentage of urea can not be read until after twenty minutes or half an hour.

For all clinical purposes the above method is perfectly sufficient and no other is required. For accurate scientific work, however, more elaborate methods are necessary, and of these the method of Mörner and Sjöqvist gives the most accurate results. If urine is treated with a mixture of barium chloride and barium hydrate and then allowed to stand under alcohol-ether for twenty-four hours, all the nitrogenous constituents of the urine are precipitated, while the urea is dissolved in the alcohol-ether. The urea solution is filtered off and the nitrogen content of the filtrate determined by Kjeldahl's nitrogen method, which consists in converting all the nitrogenous constituents of the urine into ammonia by boiling the urine with concentrated sulphuric acid. The ammonia combines with the sulphuric acid to ammonium sulphate; caustic soda is then added to liberate ammonia gas, which is distilled off into a known amount of sulphuric acid. The amount of uncombined sulphuric acid is next determined and subtracted from the known total. The difference equals the amount neutralized by ammonia, and from this factor the amount of urea is calculated. The method is too complicated for clinical work.

Urease Methods.—In 1913 E. K. Marshall introduced a new method for the determination of urea, which is based on a different principle and which is considered to be more accurate than the hypobromite method, even though it is not quite as simple. He took advantage of a discovery by Takeuchi in 1909, that an aqueous extract of soy bean, (*Glycine hispida*) contains a ferment which converts urea into ammonium carbonate. This enzyme is called urease, and its action is not interfered with by the presence of either protein or glucose. Later urease was also found in other beans, notably the Jack bean (*Canavalia ensiformis.*) It can be obtained in the form of a soluble dry powder or in the form of soluble tablets.

Different methods have been described, the simplest being the so-called "Clinical Method" of *Marshall*, which has been somewhat modified in accordance with the kind of urease employed. In the execution of this method, measure into each of two 200 c.c. Erlenmeyer flasks 5 c.c. of the urine to be examined and about 100 c.c. of distilled water. To one of these flasks add 1 c.c. of a 10 per cent. solution of urease or 1 tablet and to each a few drops of toluene. Stopper both flasks with corks, and allow them to remain at room temperature for at least eight hours, or in the incubator at 37° C. for three hours. The time required for complete hydrolysis of the urea depends on the quantity of urine used, the concentration of the urea, the amount of enzyme present and the temperature of action. The velocity of the reaction is approximately twice as rapid at 35° C. as at 25° C., and directly proportional to the enzyme concentration within certain limits. If rapid determinations are desired 1 c.c. of urine only should be used and one or two tablets of Urease added. Dilute with 100 c.c. of water and digest between 40 and 50° C. for 15 to 30 minutes. At the end of the proper time titrate the contents of each flask to a distinct pink color with decinormal hydrochloric acid, using a few drops of 0.5 per cent methyl orange solution as indicator. The amount of acid required to neutralize the urease-treated specimen, less the amount required for the control, will give the urea content estimated upon its equivalent in ammonium carbonate. The difference between the number of c.c. of decinormal acid used in the two titrations, multiplied by the factor 0.06 gives the percentage of urea in the urine. From the percentage the 24-hour elimination can be calculated.

A more accurate method is that of *Van Slyke and Cullen*, which consists in treating the urine sample with urease, aerating the ammonia formed into fiftieth-normal acid and titrating back the excess acid. A suction-pump, such as can be attached to any tap with fair water-pressure, is required. This method is somewhat too complicated.

Ammonia.—Ammonia (NH_3) is next to urea the most important nitrogenous product of protein metabolism, and is for this reason placed with the nitrogenous bodies, although it chemically belongs to the class of inorganic constituents. It is constantly present in small amounts in normal urine, varying from 0.4 to 1.2 gm. (7 to 20 grains), with an average of 0.7 to 0.8 gm. in twenty-four hours on a mixed diet. This represents from 3.5 to 5 per cent of the total nitrogen output. It is present in combination with various acids and represents a portion of the nitrogen which has not been transformed into urea, but has been utilized to combine with acid substances formed in the protein metabolism of the body. An increased production of acid in the system leads to an increased elimination of ammonia.

Under normal conditions the relation of ammonia to the total nitrogen is a fairly constant one, and varies with the diet. A pronounced reduction of total nitrogen, however, is, according to Folin, always accompanied by a relative increase in the ammonia. The term "ammonia coefficient" is sometimes used to denote the percentage of ammonia nitrogen with reference to the total nitrogen. Copious water drinking increases the ammonia output.

In diseased conditions the elimination of ammonia is increased in oxygen starvation; in febrile conditions; in diabetes mellitus where diacetic acid and β-hydroxybutyric acid are found in the urine in combination with the ammonia; in diseases of the liver when the formation of urea is interfered with, such as cirrhosis, carcinoma, and acute yellow atrophy; in uremia; in acid intoxications generally; and in the toxæmias of pregnancy, especially in cases of pernicious vomiting The elimination is diminished in many cases of nephritis, and in some cases of carcinoma of the stomach.

For the quantitative determination of ammonia a simple method is the *formalin method.* This depends upon the fact that free ammonia, when treated with formaldehyde, combines with it, with the formation of hexamethylen-tetramin, the ammonia being liberated from its salts by means of sodium hydroxide. The method is the following: Dilute 20 c.c. of urine with 60 or 100 c.c. of water, add a few crystals of neutral potassium oxalate and a few drops of a one per cent alcoholic solution of phenolphthalein. A decinormal solution of sodium hydroxide (4 gm. in litre), is added slowly from a burette, while stirring, until a permanent pink color appears. Then add 2 c.c. of a forty per cent solution of formaldehyde, which has been previously neutralized. When the pink color has disappeared, pass in more of the decinormal sodium hydroxide, until the color returns. Each cubic centimetre used in this second titration represents 0.0017 gm. of ammonia in 20 c.c. of urine. Knowing the amount of urine voided in twenty-four hours, the total daily ammonia can be easily calculated.

Uric Acid.—Uric acid ($C_5H_4N_4O_3$), like urea, is a nitrogenous product, although it is normally found in urine in small amount only, 0.3 to 1.5 gm. (5 to 25 grains) being the amount usually voided in twenty-four hours; the average is 0.7 gm. Like urea, the amount excreted is dependent upon the diet, and under normal conditions is in direct proportion to the amount of urea excreted; the proportion is 1 of uric acid to 45, 50 or 60 of urea.

Uric acid is probably formed chiefly in the liver and to a small degree in the spleen, but not in the kidneys, being only excreted by the kidneys. Recent researches tend to show that it is derived from the nucleins, the chief chemical constituent of all cell nuclei; foods rich in nucleins give rise to the formation of uric acid. Its excretion is increased by a diet rich in protein matter, especially with diminished exercise or sedentary habits; in acute fevers; diseases of the lungs and heart accompanied by dyspnœa; abdominal tumors which impede respiration; rheumatism; in severe blood diseases, especially leukæmia, in which there is a disintegration of the nuclei of the blood corpuscles. Its increase in gout has been rendered doubtful by recent investigations, as it has been found that such an increase does not always take place. After the administration of certain drugs, such as salicylates, lithium, and alkaline citrates, the elimination may also be increased. Uric acid is diminished by a vegetable diet; in chronic kidney diseases and other diseases in which the amount of urea is decreased; after the administration of different drugs, such as quinine, antipyrin, caffeine, iron, and lead.

Pure uric acid is a white, odorless substance, feebly soluble in water, insoluble in alcohol and ether, readily soluble in glycerin and alkalies. It is not acid in reaction when tested with litmus paper. It crystallizes in urine in many different forms, almost invariably of yellow or yellowish-red color; the difference in its appearance under the microscope is due to the degree of acidity of the urine, the concentration, the amount of pigments, the temperature, and the rapidity of the process of crystallization.

Under ordinary circumstances uric acid does not appear in the urine in a free condition, but always in combination with bases, such as sodium and ammonium, in the form of urates; of these bases, some are acid, others neutral. When the urine is concentrated from want of a solvent, or when poor in mineral salts which also act as solvents, or when pigments are deficient, precipitation occurs promptly upon cooling of the urine, and this also takes place when the urine is highly acid; the acidity is quickly neutralized by the bases of the urates, thereby liberating the acid. The mixed precipitate in the urine is always colored by uroerythrin: the free acid most, the ammonium urate about as much, the sodium urate less. The sodium urate occurs in characteristic granular masses, having the appearance of moss; the ammonium urate as globular formations, at times with variously sized spicules. For the reasons stated above, the amount of uric acid in the urine should not be considered excessive from the fact of a deposit forming upon cooling, as such a deposit may occur when the amount is small, and a true increase can be detected only by quantitative tests.

The detection of uric acid is easy with the aid of the microscope, owing to the characteristic lozenge-shaped, rhomboidal, wedge- or whetstone-shaped, barrel-shaped, and comb-shaped, yellowish crystals. The urates can also be easily distinguished under the microscope.

A simple test is the *murexide test*: A small portion of the sediment, or the residue after evaporation, is placed on a porcelain dish, a few drops of a strong solution of nitric acid are added, and the solution is carefully warmed. When dry, a few drops of ammonia are added, and a beautiful purple color at once appears, which soon spreads over the dish, and changes into violet upon the addition of caustic potash. The color disappears upon warming.

In this test alloxan is formed by the addition of nitric acid to uric acid or urates, and, by continuing the addition of nitric acid, alloxantin forms; this combines with ammonia to form acid ammonium purpurate, $C_8H_8N_6O_6$, also called murexide.

Another simple method for the detection of uric acid is the following. Place about 200 c.c. of filtered urine in a beaker, and acidulate it with 5 to 10 c.c. of concentrated hydrochloric acid; after stirring thoroughly, stand the vessel in a cold place for from eighteen to twenty-four hours. At the end of that time a deposit of uric acid crystals has usually appeared.

For the quantitative estimation of uric acid a convenient method is *Ruhemann's method*, which, although it does not give accurate results, is simple and practical, and may be used for general clinical purposes to determine the approximate amount of uric acid. It depends upon the decolorization of an iodine solution by the uric acid with the aid of carbon disulphide, and the measurement of the amount of urine which must be added to a definite amount of iodine solution to bring about the decolorization. For this test a graduated tube with a glass stopper, *Ruhemann's uricometer*, 25 cm. in length, is used (see Fig. 11). The reagents necessary are first, carbon disulphide, and second, an iodine solution composed of iodine, 0.5 gm., potassium iodide, 1.25 gm., absolute alcohol, 7.5 c.c., glycerine, 5 c.c., distilled water, q.s. 100 c.c.

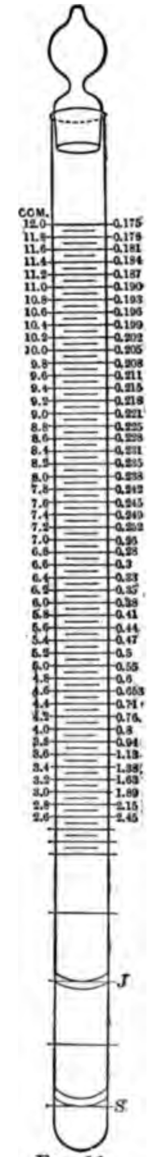

Fig. 11.—Ruhemann's Uricometer.

Place carbon disulphide in the tube to the lowest mark *S*, so that the lower meniscus of the reagent touches the mark; then slowly add the iodine solution to the mark *J*, so that the upper part of the meniscus rests upon the mark, and enough urine, by means of a pipette, to the lowest number on the tube, 2.45. Insert the glass stopper, mix the contents of the tube thoroughly, and then add more urine, drop by drop, mixing after each addition. The carbon disulphide absorbs the iodine, becoming first copper-brown, then after the addition of more urine violet, purple, pink, pale pink, and finally milky white or porcelain-white. The end-reaction is shown by the pale pink color in the carbon disulphide; this, upon more shaking, assumes a porcelain-white appearance. This process requires from six to ten or fifteen minutes, as it is best to shake the tube for about fifteen seconds after each urine addition. The amount of uric acid is then read off directly from the scale on the right, which shows the number of parts of uric acid per 1,000 of urine, or grams per litre. The scale on the left shows the number of cubic centimeters of urine used; this scale, being of little importance, is omitted from some of the uricometers.

If the urine contains very little uric acid, only half the amount of iodine solution should be used, the rest of the space to the mark *J* being filled with distilled water, the indicated amount on the tube being then divided by two. If, on the other hand, an excess of uric acid is present, twice the amount of iodine is used, and the result multiplied by two.

For this test the urine must be acid in reaction and should be free from sugar and albumin. The presence of sugar, however, interferes very little, if at all, with the result, nor does the presence of small amounts of albumin. When albumin is present in large amounts, it should first be removed by boiling, acidifying with acetic acid and filtering. Should the urine react alkaline, it must first be acidified with dilute acetic acid.

Another method for the quantitative estimation of uric acid is that of *Heintz*. This method is the following: To 200 c.c of filtered urine free from albumin add 10 c.c. of concentrated hydrochloric acid; allow to stand for twenty-four to thirty-six hours in a cool place; collect the precipitated uric-acid crystals on a previously weighed filter and wash in cold distilled water. Dry the filter and uric-acid crystals in a desiccator and weigh. By subtracting the weight of the filter, the weight of the uric acid in 200 c.c. of urine is obtained.

Purin Bodies.—The term *purin bodies,* is a collective name used for a group of bodies, which are derived from nucleins and found in urine. To this group belong uric acid, xanthin, methylxanthin, heteroxanthin, hypoxanthin, paraxanthin, adenin, guanin, epiguanin, carnin and episarcin. The most important of these substances next to uric acid is xanthin. With the exception of uric acid, all its members are basic, and are known as purin bases, alloxur bases, xanthin bases and nuclein bases. The relation between these bodies is a close one, and the differences between them but small. All originate in the theoretical purin "nucleus," of the formula C_5N_4, which yields *purin* by the addition of four atoms of H = $C_5N_4H_4$. Purin plus one atom O = hypoxanthin, plus O_2 = xanthin, plus O_3 = uric acid, which is therefore best named tri-oxy-purin. If the amido group (NH_2) replaces one H in purin, amidopurin or adenin results, and this body plus O = guanin.

There are two varieties of purin bodies in the urine; the one variety, known as "exogenous," is derived from the food and varies according to the character and amount of food taken, while the other variety, known as "endogenous," is derived from the decomposition of the nucleins of the tissue cells. These bases are found in the urine in minute amount only. Pathologically they are increased in nephritis, leukæmia, and acute yellow atrophy of the liver.

Xanthin, the most important substance of this group, is chemically closely allied to uric acid, containing one atom less of oxygen ($C_5H_4N_4O_2$) than uric acid. It crystallizes in the form of small, colorless, lozenge-shaped crystals or hexagonal plates, and differs from uric acid by its solubility in ammonia and hydrochloric acid as well as by heat.

After the addition of acetic acid under the cover glass the crystals retain their form.

Creatinin.—*Creatinin* ($C_4H_7N_3O$) is a normal constituent of urine, being excreted in small amount, from 0.6 to 1.2 gm. in twenty-four hours. It, as well as *creatin* ($C_4H_9N_3O_2$), which is occasionally found in normal urine, is derived from muscle tissue of the body and from meat taken as food, so that its amount is largely dependent upon the diet. Muscular activity increases the excretion of creatinin. Pathologically it is increased in acute diseases, such as typhoid fever and pneumonia, also in diabetes, and is diminished in conditions of wasting.

The simplest test is Jaffe's method, which consists in treating the urine with a few drops of a ten per cent picric-acid and a ten per cent sodium-hydroxide solution; if appreciable quantities of creatinin are present, the liquid at once turns red, which color remains for some time, but changes to yellow if glacial acetic acid be added. Glucose gives a similar red color, but only upon the application of heat.

Another simple and even more sensitive test is Weyl's method. To a few cubic centimetres of urine in a test tube add a few drops of a weak sodium nitro-prusside solution and render the solution alkaline with sodium or potassium hydroxide. A ruby-red color immediately appears, which, after a few minutes, changes to an intense yellow.

Hippuric Acid.—*Hippuric acid* ($C_9H_9NO_3$), normally present in urine in small amounts only, is increased after the ingestion of different fruits, such as cranberries, plums, and prunes, as well as after the administration of different drugs, such as benzoic acid, salicylic acid, cinnamic acid, and oil of bitter almonds. Meat diet diminishes its excretion, and it is quite abundant in the urine of herbivorous, absent in that of carnivorous, animals. Pathologically it is increased in intestinal putrefaction and in fevers, but its clinical significance is small. It is formed by a union of benzoic acid and glycocoll in the kidney and intestines.

Hippuric acid may be detected by boiling the urine with concentrated nitric acid and evaporating to dryness. The residue heated in the test tube gives the odor of bitter almonds, due to nitrobenzol.

Besides hippuric acid, the so-called undetermined nitrogen includes the amino acids, oxyproteic and alloxyproteic acids and allantoin.

Amino Acids.—Both *mono-* and *di-amino acids* are found in normal urine in minute quantities, when the nitrogen intake has been large. They are decomposition products of protein metabolism and are usually converted into urea in the liver. In all conditions in which the function of the liver is impaired, they are present in the urine in larger amounts. The presence of the two mono-aminu acids, leucin and tyrosin, has been especially associated with acute yellow atrophy of the liver and phosphoric acid poisoning, but they may be found in the urine in any pathological condition of the liver. The amino acids are also found in cases of pneumonia, especially during the absorption of the exudates, as well as in diabetes, gout, and leukæmia.

Oxyproteic and Alloxyproteic Acids.—These acids are constant constituents of normal urine, derived from protein metabolism. Both contain sulphur, but are of little practical importance, although it has been claimed that they are accountable for Ehrlich's diazo-reaction.

Allantoin.—*Allantoin* ($C_4H_6N_4O_3$) is a product of oxidation of uric acid. It is usually present in the urine in traces only, but is increased by a meat diet, especially one rich in nucleins. In the urine of new-born infants and during the first week of life it is more abundantly found, also not infrequently in women during pregnancy. Pathologically it is increased in cases of diabetes insipidus and hysteria, especially those associated with convulsions.

Ethereal Sulphates.—The important substances of this group are phenol, cresol, pyrocatechin, indol, and skatol. These bodies, as a rule, appear in the urine as the sodium or potassium salts of the ethereal sulphates. Indol and skatol are not eliminated as indol- or skatol-sulphuric acid, but undergo preliminary oxidation to indoxyl and skatoxyl, appearing in the urine as the sodium or potassium salts of indoxyl-sulphuric acid (indican) and of skatoxyl-sulphuric acid. The ethereal sulphates are products of decomposition, and the amount normally excreted in the urine varies with the extent of putrefaction in the intestines, as well as according to the character of the food. Their proportion to that of the total sulphates of the urine is about one to ten. They are increased whenever putrefactive processes exist in any part of the body, such as putrid pus cavities and gangrenous tissues; their amount is proportional to the severity of the putrefaction, being increased by the retention and diminished by the discharge of putrid matter. They are also increased after the use of certain drugs, such as carbolic acid and lysol, internally or externally.

Phenol and cresol may be detected in the urine by adding strong nitric acid and boiling, when an obor of bitter almonds will develop. After cooling, add bromine water; a yellow crystalline precipitate of tribromphenol appears upon standing. If a portion of the original test is rendered strongly alkaline by the addition of sodium hydroxide, an orange-red color is observed, due to the formation of sodium nitro-phenol.

Coloring Matters.—Normal urine contains a number of coloring matters as well as so-called *chromogens*, which, though colorless, readily become colored by oxidation.

Urochrome is the yellow pigment which gives the normal amber color to the urine. It can be isolated as a brown, easily soluble powder, giving yellow solutions in water and alcohol. It is precipitated by different acids.

Hæmatoporphyrin is present in minute quantities in normal urine; it is an iron-free derivative of hæmoglobin. It is increased in croupous pneumonia, pulmonary tuberculosis, pericarditis, exophthalmic goitre, Addison's disease, rheumatism and gout, lead-poisoning, and paroxysmal hæmoglobinuria, also after prolonged use of sulphonal and trional or in acute poisoning with these drugs. Urine containing larger quantities of hæmatoporphyrin has a dark wine-red, bluish-red, or even almost black color.

Uroerythrin, the pigment that gives the pink color to urate deposits, is of no practical importance, while *urohæmatin* is a derivative of hæmoglobin and is probably derived from the disintegration of hæmoglobin.

Urobilin is not usually present in freshly voided urine, but a small quantity soon forms on standing from oxidation of urobilinogen, a chromogen, which is present in fresh urine. It is formed by the reducing action of putrefactive intestinal bacteria on the bile pigments, and is greatly increased in diseases accompanied by marked destruction of red blood corpuscles or extravasation of blood into the tissues, such as pernicious anæmia, purpura, scurvy, cerebral apoplexy, and hemorrhagic infarcts. It is also increased in many febrile diseases, septic conditions, acute articular rheumatism, pneumonia, malaria, scarlet fever, diseases of the liver and bile ducts, as well as in lead colic, and has been found after administration of antipyrin and antifebrin.

Detection of urobilin: Fill a test tube three-quarters with urine and add one drop of hydrochloric acid and 5 c.c. of amyl alcohol. Shake gently a few times, allow to stand a few minutes, pipette off layer of alcohol into another test tube, dilute with two volumes ninety-five per cent. ethyl alcohol, add one drop of ammonia water to neutralize the acid added at first, and 1 c.c. five per cent. alcoholic solution of zinc chloride. Filter off any precipitate of zinc hydroxide and observe a green fluorescence of the filtrate in the presence of urobilin, destroyed by the slightest trace of acid.

Of other organic constituents of normal urine, *oxalic acid* may be mentioned. It is present in very small quantities, but is increased whenever there is an interference with oxidation in the body, being found in diseases of the heart, lungs, and liver, as well as in diabetes. It usually occurs in the form of calcium oxalate, a salt which crystallizes and is deposited in the urinary sediment when it is present in excess. The significance of oxaluria is discussed in the chapter on crystalline and amorphous sediments. Different *volatile fatty acids* are also present in minute amounts; the most important of these are formic, acetic, butyric and propionic acids. They are increased in some febrile conditions, and such an increase is known as *lipaciduria*. *Ferments*, such as pepsin and lipase are frequently present, but in traces only, likewise *aromatic oxyacids*.

B. INORGANIC.

The chief inorganic constituents of urine are the chlorides, phosphates, and sulphates which occur in combination with potassium, sodium, ammonium, calcium, and magnesium. In addition to these there are small amounts of carbonates and minute quantities of iron, fluorin, silicic acid, and free gases, including nitrogen, carbonic acid, and traces of oxygen. The total amount of inorganic substances excreted in twenty-four hours is between 12 and 27 gm.

Chlorides.—Next to urea, the chlorides are the chief solid constituents of the urine. The most important and most abundant of the chlorides is chloride of sodium, but small quantities of chloride of potassium and ammonium are also present. The amount of the chlorides voided varies considerably with the diet, being derived from the food, and they are most abundant when a large amount of salty food is ingested. The average quantity voided is between 10 and 16 gm. (2½ to 4 drachms) in twenty-four hours; a milk diet considerably reduces this amount, while an abundance of salty food may increase it to 30 or 40 gm. In starvation the chlorides almost entirely disappear from the urine. When starvation is followed by feeding, they do not appear again until the system has reabsorbed the amount voided when starvation began.

The excretion of chlorides is diminished in all febrile conditions, especially in those in which a serous exudate is formed. In pneumonia their excretion is greatly reduced during the florid stages of the disease, but rapidly increases when the exudate becomes absorbed and convalescence sets in. The chlorides are also diminished in diarrhœa and may sink to a minimum in severe gastric disorders, such as ulcer and cancer, in which very little food is taken. In chronic diseases accompanied by œdema, such as chronic nephritis, the chlorides are considerably diminished, and if the fluid is absorbed they gradually rise. In nephritis the chloride excretion usually follows the same course as the urea excretion. The chlorides are increased during active exercise and, as a rule, in diabetes, both mellitus and insipidus.

The chlorides may be detected by treating the urine with nitric acid and adding a solution of nitrate of silver; a cheesy precipitate, soluble in ammonia, shows the presence of chlorides. A test of the approximate amount of chlorides present may be made with this method, as follows: To a small amount of urine in a test tube add a few drops of nitric acid, and to this one or two drops of a nitrate-of-silver solution, one part to eight. If a white, flaky precipitate is formed, which quickly sinks to the bottom of the test tube without diffusing through the urine, the chlorides are present in normal amount (from one-half to one per cent). If a simple cloudiness appears, readily diffusing through the urine without the appearance of flakes, the chlorides are diminished to one-tenth per cent; and if no precipitate whatever is formed, they are entirely absent. If more than a trace of albumin is present it should be removed by heat before applying this test, as albuminate of silver forms and interferes with the reaction.

For quantitative estimation Mohr's titration method with silver nitrate can be used. The solutions required are:

1. Standard nitrate-of-silver solution: Dissolve 29.075 gm. of fused nitrate of silver in 1,000 c.c. of distilled water; 1 c.c. of this solution is equal to 0.01 of sodium chloride.

2. A saturated watery solution of neutral potassium chromate, made by dissolving one part of the salt in five parts of water.

Take 10 c.c. of urine; dilute with 50 c.c. of distilled water; add 8 to 10 drops of potassium-chromate solution; to this mixture add the standard silver solution drop by drop from a burette. The chlorine combines with the silver to form a silver chloride in the form of a white precipitate. When all the chlorine is precipitated, silver chromate, red in color, forms, and the silver-nitrate solution must be added until a pink tinge appears. The number of cubic centimetres of silver solution used, multiplied by 0.01, will give the amount of chlorides in 10 c.c. of urine, from which the total for twenty-four hours is calculated.

Phosphates.—Phosphates are found in the urine as salts of sodium, potassium, calcium, and magnesium. The combinations of phosphoric acid with sodium and potassium constitute the alkaline phosphates; the combinations with calcium and magnesium the earthy phosphates. The phosphoric-acid excretion is usually expressed in terms of P_2O_5; that is, phosphoric-acid anhydride; and the amount voided in twenty-four hours varies from 2.3 to 5 gm., the average being

3.5 gm. (less than one drachm). Of this amount about two-thirds is in combination with sodium and potassium (sixty per cent of which is acid sodium phosphate), and one-third in combination with calcium and magnesium. A minute amount is present as glycero-phosphoric acid.

The alkaline phosphates are soluble in water and alkalies, while the earthy phosphates are insoluble in water and are held in solution in acid urine, but are precipitated in alkaline urine, forming a sediment more marked if heat be applied. On heating a faintly acid, amphoteric, or alkaline urine, a precipitate forms, which may be mistaken for albumin; from this it may be easily distinguished by the addition of two or three drops of an acid, such as acetic or nitric, which quickly dissolves the earthy phosphates. If the magnesium phosphate be acted upon by ammonia, the ammonio-magnesium phosphate—so-called triple phosphate—is formed.

The phosphates in the urine are derived partly from the food, partly from the decomposition of organic substances containing phosphorus, such as nuclein and lecithin; they are more abundant after an animal, less abundant after a vegetable, diet. A continued increase in the total amount of phosphates in the urine is spoken of as phosphaturia. A diagnosis of this condition is usually based upon the presence in the urine of a dense deposit of phosphates; analyses of many of these cases, however, do not show an increased amount of phosphoric acid, but merely a diminished acidity of the urine, and the diagnosis of phosphaturia should not be applied to them.

The amount of phosphates excreted in the urine is increased in diabetes mellitus, in diseases of the bone, such as osteomalacia and rachitis, in diseases of the nerve centres, and in destructive pulmonary diseases, such as tuberculosis. It is diminished in severe diseases of the kidney, in a variety of acute infections such as pneumonia at the height of the disease, in different chronic diseases, and during pregnancy, probably due to the formation of the fœtal bones, sometimes also in gout.

A condition known as *phosphatic diabetes*, and considered to be an independent disease of metabolism has been described. In this condition the symptoms are similar to those in diabetes mellitus with a polyuria and a continuous large increase of phosphates in the urine as high as 10 gm. or more in twenty-four hours, but without a glycosuria. In true diabetes mellitus the phosphates may be increased at one time and diminished at another, there frequently being an inverse ratio between the excretion of sugar and phosphates.

The earthy phosphates may be detected by rendering the urine strongly alkaline with ammonia or caustic potash and gently heating, which causes their precipitation in the form of a whitish cloud of feathery flakes that settles to the bottom of the test tube. The precipitate is dissolved on the addition of acetic acid. To detect the alkaline phosphates, remove the earthy phosphates by precipitation and filter. To a given quantity of the filtrate add one-third the quantity of magnesian fluid (1 part each of magnesium sulphate and ammonium chloride, 8 parts of distilled water, and 1 part of liquor ammoniæ). The alkaline phosphates are precipitated in the form of a snow-white deposit. If the entire fluid presents a milk-like, cloudy appearance, the alkaline phosphates are present in normal amount; if it is denser and more cream-like, there is an increase; but if the fluid is only slightly cloudy or remains transparent, the phosphates are diminished.

To estimate the amount of total phosphoric acid in the urine, the best method is that of titration with uranium nitrate or acetate. It is based upon the fact that a solution of a phosphate acidulated with acetic acid, when treated with a uranium nitrate or acetate solution gives a yellowish-white precipitate of uranium phosphate, and when a soluble salt of uranium is added to a solution of potassium ferrocyanide, a reddish-brown precipitate develops. The solutions required are:

1. A standard solution of uranium nitrate or acetate, consisting of 35.5 gm. of the salt to 1,000 c.c. of distilled water; 1 c.c. corresponds to 5 mgm. of phosphoric anhydride.

2. Sodium-acetate solution, 100 gm. of sodium acetate being dissolved in 900 c.c. of water, and to this mixture 100 c.c. of a thirty per cent solution of acetic acid being added.

3. A saturated solution of potassium ferrocyanide, to be used as an indicator.

To 50 c.c. of the urine in a glass beaker add 5 c.c. of the sodium-acetate solution. Heat over a water bath and add the uranium solution drop by drop, as long as a precipitate forms or until a drop of the mixture, placed upon a porcelain plate, gives a distinct brown color with a drop of potassium ferrocyanide. The number of cubic centimetres of the uranium solution is then read off and multiplied by 0.005 (5 mgm.), which gives the amount of phosphoric acid in 50 c.c. of urine; from this the quantity in twenty-four hours is calculated. The end reaction, shown by the brown color on the porcelain dish, takes place when the uranium solution has precipitated all the phosphoric acid and is present in excess.

Instead of potassium ferrocyanide as an indicator, cochineal tincture may be used. A few drops of it are added to the urine before heating, and the standard uranium solution is then added until a faint, but distinct and permanent green color appears; this color begins to appear as soon as all the phosphoric acid has been precipitated, and there is a slight excess of uranium. This indicator has the advantage that it may be added directly to the urine before heating.

To estimate the amount of phosphoric acid in combination with calcium and magnesium, that is the earthy phosphates, the following method may be used: To 100 c.c. of urine in a beaker add an excess of ammonium hydroxide and allow the mixture to stand for from twelve to twenty-four hours. The phosphoric acid in combination with the alkaline earths, calcium and magnesium, is precipitated as phosphates of these metals under these conditions. Collect the precipitate on a filter paper and wash it with dilute ammonia water (1 to 3). The filter is then pierced, the precipitate washed down with hot water into a beaker, and dissolved while warm with a small amount of dilute acetic acid. Bring the volume up to 50 c.c. with water, and add 5 c.c. of sodium acetate. Now proceed as in the preceding method. The difference between the total amount of phosphoric acid and that in combination with the alkaline earths, represents the quantity combined with the alkalies, that is the alkaline phosphates.

Sulphates.—The sulphates occurring in the urine are of three kinds: first, the preformed, mineral or inorganic sulphates, which occur as compounds of sodium, potassium, calcium, and magnesium, the former predominating; second, the neutral sulphates, unoxidized or organic sulphur, excreted as a constituent of such bodies as cystine, taurine, sulphocyanates, hydrogen sulphide, oxyproteic acid, alloxyproteic acid, and uroferric acid; third, the ethereal sulphates, also known as the aromatic or conjugate sulphates, that is sulphuric acid in combination with aromatic bodies, such as phenol, indol, skatol, cresol, pyrocatechin, and hydrochinon. The first two form about ninety per cent, the third about ten per cent of the total sulphuric acid.

The quantity excreted by the kidneys varies from 1.5 to 3 gm. (23 to 45 grains) in twenty-four hours. Sulphates are extremely soluble and are never met with in the form of deposits, excepting calcium sulphate. They are derived partly from the food and partly from the decomposition of proteins in the tissues. The total quantity bears a fairly constant relation to total nitrogen, being one to five.

An increased excretion of sulphates takes place after a meat diet and as a result of active exercise; this is also the case in acute fevers with an increased excretion of urea. After taking sulphuric acid or sulphates and after the inhalation of oxygen, they are likewise increased. Sulphates are diminished after a strictly vegetable diet, in nephritis, in convalescence from acute diseases, and in all conditions associated with diminished metabolism.

Sulphates may be detected by adding to a given quantity of urine in a test tube one-third as much of an acidulated solution of barium chloride (4 parts of barium chloride, 16 parts of distilled water, 1 part of concentrated hydrochloric acid). An opaque, milky cloudiness will appear when the amount of the sulphates is normal. If the opacity is intense and the mixture has the appearance of cream, the sulphates are increased; but if there is only a slight cloudiness, they are diminished.

To estimate the amount of total sulphates the volumetric method may be employed. The following solutions are required:

1. A standard solution of barium chloride, made by dissolving 30.54 gm. of crystallized barium chloride in 1,000 c.c. of distilled water; 1 c.c. of this solution corresponds to 0.01 gm. of sulphuric-acid anhydride (SO_3).

2. A solution of potassium sulphate, containing 21.778 gm. of the salt in 1,000 c.c. of water.

3. Pure hydrochloric acid.

One hundred cubic centimetres of urine are rendered acid by the addition of 5 to 10 c.c. of hydrochloric acid and heated to boiling in a flask. The barium-chloride solution is allowed to drop into the mixture as long as any precipitate occurs, the mixture being heated before each addition of the barium solution. After adding 5 to 8 c.c. of the solution, allow the precipitate to settle; filter a small portion of the mixture and add a few drops of the standard solution. If any precipitate occurs, return the whole to the flask, add more barium solution, and test as before, until no more precipitate is formed on the addition of barium chloride. An excess of the latter should be avoided.

If only a trace of excess is present, a drop of the clear fluid removed from the flask gives a cloudiness with a drop of potassium-sulphate solution placed on a glass plate over a black background. If more than a cloudiness appears, too much barium chloride has been added, and the test must be repeated. From the amount of barium chloride used, the percentage of sulphuric acid in the urine is calculated, 1 c.c. of barium-chloride solution corresponding to 0.01 gm. of SO_3.

Carbonates.—In urine of an alkaline reaction minute quantities of carbonate and bicarbonate of ammonium, calcium, sodium, and magnesium are present. As a result of alkaline decomposition of the urine, ammonium carbonate may be found in large quantities. The carbonates are derived from the food, especially from vegetable acids, and may be considerably increased after drinking alkaline mineral waters. An excess of carbonates renders the urine turbid when passed, or it becomes so upon standing, and upon sedimentation the precipitate is that of calcium carbonate, usually associated with phosphates.

The presence of carbonates in the urine is detected by the evolution of gas, upon the addition of a few drops of an acid, such as acetic or nitric.

Other inorganic constituents, such as iron, silicic acid, fluorin, and hydrogen dioxide, occur in normal urine in traces only, and are of no clinical importance.

Centrifugal Analysis.

Centrifugal Analysis.—The method of centrifugal analysis for the ready approximate determination of bulk percentages of chlorides, phosphates, and sulphates, as well as of albumin was introduced by Purdy. While by no means accurate, this method is a convenient one and has the advantage over other methods for quantitative estimation of yielding quick results, which are sufficiently accurate for clinical work. From the bulk percentages Purdy has determined weight percentages.

Purdy advises the use of an electrical centrifuge possessing a radius of arm and tube of 6¾ inches, accurately graduated percentage tubes, with a capacity of 15 c.c. each, and a gauge to regulate the speed. He uses the double arm of the motor, carrying four tubes, so that he can estimate the bulk percentages of chlorides, phosphates and sulphates, and if necessary also of albumin at the same time. An electrical centrifuge is, however, not essential, as a well-made, single or double speed hand centrifuge gives practically the same results, provided that a uniform speed is maintained. This speed should be 1,200 or 1,500 revolutions per minute for three minutes, which is obtained by rotating the handle 50 to 60 times per minute.

Estimation of Chlorides.—Fill the percentage tubes to the 10 c.c. mark with fresh urine; add 1 c.c. (15 to 20 drops) of strong nitric acid to prevent precipitation of phosphates, and fill tube to the 15 c.c. mark with a silver nitrate solution (1 part to 8 of water). The ungraduated tube may be filled with water or urine, if no other tests are to be made. Close the tube, mix the contents thoroughly, and allow to stand for two or three minutes to secure complete precipitation; now centrifugalize for three minutes, at the rate of 1,500 revolutions per minute, after which the bulk percentage of silver chloride is read off on the scale of the tube. The normal bulk percentage of silver chloride ranges from five to eight per cent.

From the bulk percentage of silver chloride the percentage by weight both of sodium chloride and of chlorine may be calculated. Each one-tenth of a cubic centimetre of the precipitate, that is one per cent by bulk is equivalent to 0.13 per cent by weight of sodium chloride and 0.08 per cent of chlorine. If, for instance, the precipitate is five-tenths of a cubic centimetre, that is five per cent by bulk, the weight percentage of sodium chloride is 0.65, that is 6.5 gm. per litre of urine; if eight per cent by bulk, it is 1.04 or 10.4 gm. per litre; and if ten per cent by bulk, it is 1.3 or 13.0 gm. per litre.

Estimation of Phosphates.—Fill the percentage tube to the 10 c.c. mark with urine; add 2 c.c. of 50 per cent acetic acid and 3 c.c. of a five per cent uranium-nitrate solution. Close the tube, mix the contents thoroughly and allow to stand for a few minutes; now centrifugalize for three minutes at the rate of 1,500 revolutions per minute. The normal bulk percentage of uranyl phosphate is eight to ten per cent. According to Purdy the first one-tenth of a cubic centimetre of the precipitate, that is one per cent by bulk of uranyl phosphate, is equivalent to 0.04 gm. of phosphoric acid by weight in each 100 c.c. of urine. Each succeeding percentage by bulk increases by 0.01. For instance, five per cent by bulk of uranyl phosphate equals 0.08 gm. of phosphoric acid (0.04 plus 0.04) in each 100 c.c., or 0.8 gm. per litre of urine; ten per cent by bulk equals 0.13, or 1.3 gm. per litre; fourteen per cent by bulk, 0.17 or 1.7 gm. per litre.

Estimation of Sulphates.—Fill the percentage tube to the 10 c.c. mark with urine and add 5 c.c. of barium chloride solution, composed of 4 parts of barium chloride, 1 part of concentrated hydrochloric acid, and 16 parts of distilled water. Close the tube, mix the contents thoroughly, and allow to stand for a few minutes; centrifugalize for three minutes at the rate of 1,500 revolutions per minute. The normal bulk percentage of barium sulphate is about 0.8 per cent. Each one-tenth of a cubic centimetre of the precipitate, that is one per cent by bulk, is equivalent approximately to 0.25 gm. of sulphuric acid by weight in 100 c.c. of urine. For instance, one-half per cent by bulk of barium sulphate equals 0.13 gm. of sulphuric acid by weight in 100 c.c. of urine, or 1.3 gm. per litre; one per cent by bulk equals 0.25 or 2.5 gm. per litre; one and one-quarter per cent 0.31 or 3.1 gm. per litre; and 2 per cent, 0.49 or 4.9 gm. per litre.

CHAPTER V.

PROTEINS.

The term proteins or albuminous substances includes a group of substances related to each other though differing in constitution and properties. The following proteins may be found in the urine: serum-albumin, serum-globulin, nucleo-albumin, albumoses and peptone, hæmoglobin, fibrin, and rarely histon and nucleo-histon, which latter are derivatives of the cell nuclei.

The chief clinical interest centres in serum-albumin, which is frequently combined with serum-globulin, and by the term *albuminuria* the presence of these bodies in the urine, without regard to the possibility of the presence of other proteins, is usually meant.

Albuminuria.—The presence of albumin in any appreciable amount must always be regarded as a pathological phenomenon, although minute quantities, which escape detection by the ordinary clinical tests, are present in some normal urines. The detection of albumin in the urine does not necessarily signify the presence of a renal trouble, but it may be due to a variety of causes. Even a comparatively large amount may exist without any kidney lesion whatever, and it is a grave mistake to conclude that a nephritis must exist because albumin has been found. Although in the larger number of cases in which albumin is found a nephritis is present, a microscopical examination must invariably be made to determine, if possible, the exact source of the albumin; and only if pus corpuscles and kidney epithelia, with or without the presence of casts, are found, a diagnosis of a nephritis is justified.

On the other hand, a nephritis may exist and yet albumin be found in such minute quantities as occasionally to escape detection altogether. This is sometimes the case in cirrhosis of the kidney, where a large amount of albumin is rarely seen, and it may be entirely absent for a few hours. In such cases the urine of the entire twenty-four hours should be tested before concluding as to the presence of albumin.

In all cases where pus corpuscles in moderate numbers are found in the urine, albumin may always be detected, if careful tests are made, though there may be no more than a faint trace. It can thus easily be seen that in such widely different lesions as pyelitis, cystitis, prostatitis, urethritis, and vaginitis, it might be present in the urine, and a microscopical examination will be necessary to determine its origin. In hemorrhage from any portion of the genito-urinary tract, a considerable amount of albumin is usually found. The rare cases of chyluria, in which the kidney may be perfectly intact, are always associated with the presence of a large amount of albumin. These cases of extrarenal albuminuria are known as *pseudo-* or *accidental albuminuria*, to differentiate them from *renal* or *true albuminuria*.

Disturbances of circulation, due to a variety of causes, may bring about the presence of albumin without any structural changes in the kidney. Such cases are often roughly termed *functional albuminurias*. It is not always easy to trace the cause of such albuminurias, though they may be due to prolonged muscular exercise, to cold baths, mental shock, to lesions of the nervous system, or to organic heart lesions. After eating a heavy protein meal a temporary albuminuria, known as *alimentary albuminuria* may appear. Albuminuria of pregnancy, due to the pressure of the pregnant uterus, is very common, and in many of these cases an organic lesion of the kidney will develop.

Another type of functional albuminuria, known as *albuminuria of adolescence* occurs in young neurotic individuals. This as well as other forms may be *cyclic*, that is the albumin recurs periodically at certain times of the day, and is absent at other times. *Orthostatic or postural albuminuria* occurs only when the patient is in an erect posture, and disappears when he lies down.

Changes in the composition of the blood with a broken-down constitution, as seen in anæmia, tuberculosis, malaria, leukæmia, pyæmia, etc., when no lesions of the kidney can be discovered, will cause the appearance of albumin; and this may also be the case in any other febrile condition. The effect of certain poisons upon the blood, such as strychnine, pilocarpine, phosphorus, arsenic, lead, potassium chlorate, iodine, alcohol, and toxins, may cause the appearance of albumin in the urine.

Before resorting to chemical tests for the detection of albumin in the urine, it is advisable to have the urine as clear as possible, as a cloudy sample renders the detection of small quantities of albumin difficult. In many cases a simple filtration through a double layer of filter paper is sufficient. Where this does not suffice, the urine should be centrifugalized and then filtered, if necessary, a number of times. If the urine is very cloudy, filtration through a tight plug of fine asbestos filtering fibre may clear it up completely. Treating the urine with different agents, such as magnesium oxide or talcum, is not advisable, as experiments have shown that thereby, not only traces, but even considerable quantities of albumin may be removed.

Detection of Albumin in Urine.—1. HEAT TEST WITH ACETIC ACID.—The tests for albumin are quite numerous, but one of the most reliable is the following: Fill an ordinary test tube about one-fourth or one-fifth full of urine and boil thoroughly; then add two or three drops of a solution composed of equal parts of glacial acetic acid and water. If albumin is present the urine becomes cloudy, the cloudiness being the more pronounced the larger the amount of albumin.

The unboiled urine, as brought for examination, is either transparent or cloudy. When the urine is boiled the results may be the following:

(*a*) The urine is transparent, and upon boiling remains unchanged. This indicates *normal urine*.

(*b*) The urine is transparent, but after boiling becomes cloudy. By adding a few drops of acetic acid it clears up entirely. This shows the presence of an increased amount of *phosphates*. If effervescence occurs upon the addition of the acid, either calcium carbonate or ammonium carbonate (the latter being always held in solution, and never precipitated so as to be found under the microscope) is present.

(*c*) The urine is transparent, but after boiling becomes cloudy, and the cloudiness remains or becomes more pronounced upon the addition of the acid. This indicates the presence of *albumin*, which, in larger quantities, will be thrown down in flakes; when very abundant, the urine may be converted into a jelly-like mass. The acetic-acid test will show the presence of the smallest traces of albumin, though these may escape detection if not carefully observed. The best plan in such cases is to take a second test tube and pour into it unboiled urine; then compare the two test tubes by holding them against a dark background. When this is done, the faintest trace of albumin can be detected by the slight cloudiness in the test tube containing the boiled urine.

(*d*) The urine is cloudy, but upon boiling clears up entirely and remains clear upon the addition of the acid. This indicates an excess of *urates*, especially sodium urate.

(*e*) The urine is cloudy, the cloudiness disappears upon warming, but reappears and becomes more pronounced upon boiling and the addition of the acid. This shows an excess of *urates, in addition to the presence of albumin.*

(*f*) The urine is cloudy, and remains unchanged by boiling and by the addition of acetic acid. This proves the presence of *micro-organisms*, such as micrococci and bacilli.

As nucleo-albumin and mucin are also precipitated by this test, Purdy recommends the following method for performing it: Have on hand a saturated aqueous solution of sodium chloride. Fill a clean test tube about two-thirds full of the previously filtered urine, and add to this about one-sixth of its volume of the sodium-chloride solution. Next add five to ten drops of acetic acid (fifty per cent) and gently heat the upper inch or so of the contents of the test tube for about half a minute. If albumin be present, even in the minutest traces, it will appear in the upper, boiled portion of the test tube if examined in good light. For all practical purposes, however, the original test, as given above, is perfectly sufficient and is undoubtedly more accurate and sensitive than the nitric-acid test.

2. Heat Test with Nitric Acid.—A common test for albumin is the nitric-acid test, the urine being boiled and a few drops of nitric acid added. This test is not as reliable as the preceding, since, if a small amount only of albumin be present and the acid added be in excess, the albumin may become redissolved. On the other hand, if the amount of acid added is small and the phosphates are present in excess, a part only of the basic phosphates will be acidified and a soluble albuminate will be formed, which remains in solution.

3. Heller's Test.—Another frequently employed test, known simply as "the nitric-acid test," is used as follows: Place a small quantity of pure nitric acid in a test tube and allow an equal amount of clear, previously filtered urine to trickle from a pipette down the side of the inclined tube, so that the urine overlies the acid. If albumin is present, a distinct, sharp, white zone will appear at the point of contact between the acid and the urine, varying in thickness according to the amount of albumin present and according to the rapidity with which the urine is dropped into the tube. If only a trace of albumin be present, a number of minutes may elapse before the zone becomes visible.

This test can also be performed by first pouring the urine into the test tube and then allowing the nitric acid to flow down the sides of the tube; the acid, being heavier than the urine, will form a separate layer below the urine.

Other substances in the urine may give rise to the formation of a nitric-acid ring, and if care is not taken will be mistaken for the zone caused by the presence of albumin. Thus in concentrated urines urates may form a zone, which, however, does not appear at the point of contact between the acid and the urine, but above the point of contact, and spreads downward; it will disappear on heating. Uric acid and urea, if present in large amounts, may be precipitated, but are recognized by their crystalline nature. Mucin is also precipitated, but is dissolved by the excess of nitric acid at the point of contact. Nucleo-albumin and albumoses are likewise precipitated; the former gives a fainter ring than albumin, which is above the point of contact, while the ring formed by the latter disappears on heating and reappears on cooling.

4. POTASSIUM-FERROCYANIDE TEST.—To 10 c.c. of previously filtered urine add five drops of strong acetic acid. If a precipitate appears, it is due to nucleo-albumin or mucin and should be filtered off. Then add a few drops of a five to ten per cent potassium-ferrocyanide solution. If a small amount of albumin be present, a faint cloudiness at once appears; if a larger amount be present, a flocculent precipitate forms at once. Albumose also gives a cloudiness, which, however, disappears upon heating.

5. SPIEGLER'S TEST.—This test, as modified by Jolles, consists in adding to 4 or 5 c.c. of previously filtered urine 1 c.c. of a thirty per cent acetic-acid solution and 4 c.c. of the reagent. The latter is composed of 10 gm. mercuric chloride, 20 gm. succinic acid, and 20 gm. sodium chloride, in 500 c.c. of water. In adding the solutions care must be taken that they are not mixed with each other, but layered over each other. If albumin be present, a distinct, sharp, white zone, which is especially plain on holding the test tube against a dark background, at once appears.

6. SULPHO-SALICYLIC-ACID TEST.—Add two or three drops of a twenty per cent watery solution of sulpho-salicylic acid or a few small crystals of the acid to 4 or 5 c.c. of urine in a test tube, and mix thoroughly. If small amounts of albumin are present, an opalescent cloudiness appears; if larger amounts are present, a pronounced turbidity or heavy precipitate forms. Albumose is also precipitated by this test, but disappears on heating, to reappear on cooling.

7. BIURET REACTION.—The urine is first treated with a ten per cent solution of sodium or potassium hydroxide, and then a ten per cent solution of cupric sulphate is added drop by drop. If serum-albumin and globulin alone are present, the liquid turns pure violet; if albumoses and peptone alone are present, it turns rose; if several of the albumins are present together, the urine assumes tints intermediate between violet and rose. Care should be taken not to add too much cupric sulphate, since if the urine contains only small amounts of albumin, the color of the copper solution will cover the color of the biuret reaction.

8. PICRIC-ACID TEST.—To a given amount of previously filtered urine in a test tube add an equal amount of a saturated solution of

picric acid. If albumin is present, a precipitate forms, varying from a light cloud to heavy flakes, according to the amount of albumin. This test is delicate, but precipitates other substances besides serum-albumin, which, however, will disappear on heating.

For performing a number of the above-described tests, but more especially Heller's test, a small glass instrument, known as the horismascope (see Fig. 12), can conveniently be used. The urine to be tested is poured into the large tube, and the reagent into the small tube. The reagent, being of higher specific gravity than the urine, flows down the capillary tube and forms a layer under the urine. The slightest opacity at the contact point of the two fluids is easily seen against a black background.

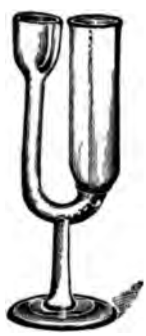

FIG. 12.—HORISMASCOPE.

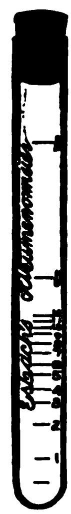

FIG. 13.—ESBACH'S ALBUMINOMETER.

Numerous tests besides these here given have been described and have found their adherents. Few authors will agree as to the most reliable test for albumin, some preferring the more delicate tests, such as Spiegler's and the sulpho-salicylic-acid tests, others Heller's and the ferrocyanide tests, still others the heat tests. For all practical purposes, the first test given—the heat and acetic-acid test—is perhaps the most reliable. If doubt remains as to the presence of albumin, any of the other tests described will clear up the question.

Quantitative Tests for Albumin.—It is of the utmost importance to have an approximate idea of the quantity of albumin present in any given case, and too many errors are constantly made in this respect. It is by no means rare to hear of a urine containing twenty-five, forty, or even fifty per cent of albumin. What is thereby meant is, of course, per volume; yet such statements are absolutely misleading. As a matter of fact, one-tenth of one per cent is a moderate amount of albumin, one-twenty-fifth of one per cent being a small amount; one-half of one per cent is a large amount, and it is only in comparatively rare cases that one per cent or more is present; more than four or five per cent is probably never found.

The simplest method of estimating the approximate amount of albumin is by means of *Esbach's albuminometer* (see Fig. 13). This instrument consists of a graduated glass tube, which is filled with urine to the letter *U* marked upon the tube, and with the test solution to the letter *R*. The latter consists of one part of picric acid to coagulate the albumin, two parts of citric acid to hold the phosphates in solution, and distilled water to make one hundred parts. The tube is now closed with the rubber stopper supplied with it, and the contents thoroughly mixed. It is then set aside for twenty-four hours to allow the precipitate to settle thoroughly, and the amount of the precipitate carefully noted. The tube contains a number of main lines of division, each one of which signifies 1 gm. of albumin in 1,000 gm.—that is, one-tenth of one per cent. Many of the instruments are only graduated for seven-tenths of one per cent, and this is sufficient for most cases. In those rare cases in which more than that amount of albumin is present, the urine must be diluted with one, two, or even three parts of water before testing. It must always be borne in mind that this method can never be absolutely accurate, since picric acid will also precipitate urates, peptone, and vegetable alkaloids; but it undoubtedly gives an approximate idea, which is all that is required in most cases.

Creatinin may be an important factor which causes errors in Esbach's instrument. An entire precipitate has been found to be a compound of potassium picrate with creatinin; it was detected by macroscopical appearance and proved by recrystallization from hot water. Albumin cannot be recrystallized, and we must guard against this possibility of results much too large by Esbach's method.

Kwilecki's Modification of Esbach's Method.—Esbach's test, although by no means accurate, is so simple that it is universally used for the clinical estimation of the amount of albumin present in the urine, the more so since it is sufficiently accurate for ordinary clinical work. Its chief drawback is the necessity of waiting twenty-four hours before precipitation is complete, and the quantity of albumin can be determined. To overcome this, Kwilecki devised a simple modification, by means of which small amounts of albumin can be estimated in two minutes, and larger quantities in five or six minutes. The method is the following: To the measured amount of urine in Esbach's tube add ten drops of a ten per cent solution of ferric chloride before the addition of Esbach's reagent. Fill the tube to the letter *R* with the reagent, mix thoroughly, and place in a water bath at a temperature of 72° C. (162° F.). The precipitation begins almost immediately and is complete at the end of a few minutes, when the result can be read off.

Tsuchiya's Method.—This is another modification of Esbach's method, which is more accurate than the latter. The reagent consists of a solution composed of 1.5 gm. of crystalline phosphotungstic acid, 5 c.c. of concentrated hydrochloric acid, and 93.5 c.c. of ninety-five per cent alcohol. The reagent is used with the Esbach tube in the same manner as the original test, and twenty-four hours are required for complete precipitation. This method gives practically no precipitate with normal urine, as is sometimes the case with Esbach's reagent, and the albuminous precipitate settles more regularly and uniformly. With small amounts of albumin this method is decidedly preferable to Esbach's.

Purdy's Centrifugal Method.—The centrifugal method, although hardly more exact than Esbach's method, is a very convenient one for a rough estimation of the amount of albumin, and is performed in a short space of time. Purdy advises the use of an electric centrifuge, the radius of which, with tubes extended, is exactly 6¾ inches. A good single- or double-speed hand centrifuge, however, gives practically the same results, provided that a uniform speed is maintained. The method is performed as follows: Fill the graduated or percentage tube to the 10 c.c. mark with urine; add 3 c.c. of a ten per cent potassium ferrocyanide solution, and 2 c.c. of a fifty per cent acetic acid solution, after which the contents of the tube should be thoroughly mixed. Allow the tube to stand for ten minutes, to insure the entire precipitation of the albumin. Now centrifugalize for three minutes at a uniform speed of 1,200 or 1,500 revolutions per minute, and read off the bulk percentage. Each $\frac{1}{10}$ c.c. of the precipitate, that is, each division of the tube, represents one per cent of albumin by measure, but not by weight.

According to Purdy, one per cent by bulk represents 0.021 per cent of albumin by weight. Purdy's table up to ten per cent is the following: ¼ per cent by the centrifuge represents 0.005 per cent by weight of dry albumin; ½ per cent, 0.01; ¾, 0.016; 1, 0.021; 1¼, 0.026; 1½, 0.031; 1¾, 0.036; 2, 0.042; 2¼, 0.047; 2½, 0.052; 2¾, 0.057; 3 per cent, 0.063; 3½, 0.073; 4, 0.083; 4½, 0.094; 5, 0.104; 5½, 0.111; 6, 0.125; 6½, 0.135; 7, 0.146; 7½, 0.156; 8, 0.167; 8½, 0.177; 9, 0.187; 9½, 0.198; and 10 per cent, 0.208.

If the amount of albumin is excessive, dilute the urine with water till the volume of albumin falls below ten per cent; multiply the result by the number of dilutions employed.

An *approximate estimation* of the amount of albumin can be obtained from the amount of precipitate in the bottom of the test tube after using the heat and acetic-acid test. A mere clouding is a faint trace, trace, or more than trace, according to the degree of the clouding; a small but perceptible precipitate is one-fortieth to one-thirtieth per cent; if the precipitate forms about one-twentieth of the column of urine, the amount of albumin is one-twentieth per cent; if it forms about one-tenth of the urine column, one-tenth per cent; one-quarter of the urine column, one-fifth to one-fourth per cent; and one-half of the urine column, two-fifths to one-half per cent of albumin.

The most exact method for the determination of the amount of albumin is the gravimetric method, which consists in coagulating the albumin either by heating or by means of chemical agents, filtering out the albumin, collecting, drying, and weighing. It is too elaborate for clinical work.

Removal of Albumin from Urine.—In a number of the general quantitative tests, it is advisable to remove the albumin if more than a trace is present. The simplest manner of doing this is to acidify the urine with acetic acid, boil until a flocculent precipitate forms and filter. The filtrate is usually clear and contains no albumin, but does contain albumoses. Hofmeister therefore recommends the following method: To a small amount of urine add 10 c.c. of a forty per cent sodium acetate solution and the same amount of a ten per cent ferric chloride solution, when a bright red color will appear. The urine is now rendered neutral or faintly acid and boiled. The albumin separates out with the basic ferric acetate and is filtered off. This method can not be used if sugar is present, in which case the urine is simply treated as first stated.

Besides serum-albumin, the urine may contain a number of similar but less important substances, among which may be mentioned globulin, albumose, peptone, mucin, and fibrin.

Globulin.—Globulin is almost always associated with serum-albumin in every albuminous urine, and its clinical significance is nearly identical with the latter. It is, however, more abundant than serum-albumin in many cases of acute nephritis and in chronic nephritis with waxy degeneration of the kidney, also in some cases of pneumonia.

Globulin can be detected by the method of Pohl in the following manner: Render the urine neutral or even faintly alkaline by the addition of ammonium hydroxide, and filter after standing one or two hours; then add an equal volume of a saturated solution of ammonium sulphate. If globulin is present, a white, flocculent precipitate forms immediately.

Another simple method depends upon its insolubility in diluted urine. Dilute a certain amount of previously filtered urine with ten times the amount of distilled water, and a flocculent precipitate appears; this is hastened by the addition of one or two drops of dilute acetic or boric acid. Or, fill a test tube with water, and allow a few drops of the albuminous urine to fall into it. If globulin is present in any quantity, each drop of urine as it falls is followed by a milky streak, and after a number of drops have been added the water assumes a milky opalescence throughout.

Albumoses and Peptones.—The term albumoses or proteoses includes a number of albuminous bodies which are intermediate products between albumin and peptone, the end-product of digested albumin. They are formed in the body by the action of the gastric and pancreatic juices. They are not coagulated by heat, but are precipitated by acids, the precipitate thus formed being redissolved by heat. The albumoses are divided into primary and secondary; the primary are proto-albumose and hemi- or hetero-albumose; the secondary are deutero-albumoses, which so closely resemble peptone in its reactions that they cannot always be differentiated from the latter.

The clinical significance of the albumoses is not yet positively known. They have been found in urine in a number of different conditions, such as ulceration of the intestines, tertiary syphilis, hemiplegia, cancer, double pneumonia, scarlet fever, diphtheria, muscular atrophy, and abscesses.

Albumoses are detected by their solubilities and reactions. Proto- and deutero-albumose are soluble in hot and cold water, while hetero-albumose is insoluble in water; all three are soluble in ten per cent solutions of sodium chloride. The primary albumoses are precipitated by strong solutions of sodium chloride and magnesium sulphate; also by saturated solutions of ammonium sulphate and by cold nitric acid. Secondary albumose is not precipitated by strong solutions of sodium chloride and magnesium sulphate, but is precipitated by ammonium sulphate; with nitric acid it is only precipitated in the presence of an excess of sodium chloride. It gives the biuret reaction previously described.

Another albumose, known as Bence-Jones albumose, differs from those just described in being coagulated by heat. It is not identical with the other albumoses, and its occurrence in urine is rare. It has been found in cases of osteomalacia and multiple sarcomata.

Peptones are the final products of gastric and pancreatic digestion. They cannot always be differentiated from albumoses, since both have many reactions in common; and the term peptonuria is not strictly correct, as albumoses and peptones are usually found together. It is a question whether true peptones ever appear in the urine alone.

These substances are frequently found in many different pathological conditions. Among these may be mentioned croupous pneumonia, pulmonary tuberculosis, gangrene of the lungs, empyema, cancer (especially of the gastro-intestinal tract and the liver), phosphorus-poisoning, septicæmia, acute yellow atrophy of the liver, typhoid fever, typhus fever, variola, scarlet fever, erysipelas, acute arthritis, and suppurative conditions generally. Some authors claim that peptone is invariably present when pus has formed somewhere in the body, and consider it of diagnostic significance in cases in which the clinical features are not sufficiently clear for a positive diagnosis. Thus it is considered possible to decide as to the presence of a purulent or a tubercular meningitis, a purulent or serous arthritis, an empyema or serous pleurisy, etc. Peptones have, however, also been found in physiological conditions, such as the involution of the pregnant uterus —so-called puerperal peptonuria or albumosuria—so that their presence does not necessarily signify a diseased condition.

Peptones are easily soluble in water, do not coagulate by heat, and do not precipitate by the addition of most of the reagents used for the detection of albumin, such as acetic acid, nitric acid, and potassium ferrocyanide. They are precipitated by tannin, potassio-mercuric iodide, picric acid, and phosphotungstic acid.

They may be detected by the following method: To urine which has been slightly acidified by acetic acid, add a saturated solution of magnesium or ammonium sulphate, and filter out any precipitate formed, which may consist of albumin, globulin, or the albumoses. If potassio-mercuric iodide or picric acid is now added and a precipitate occurs, it consists of peptone.

Another test is the following: 10 c.c. of urine are acidified with one or two drops of hydrochloric acid, the mixture precipitated with a five or ten per cent solution of phosphotungstic acid, and heated. The supernatent fluid is poured off and the precipitate dissolved in a few cubic centimetres of distilled water to which a small amount of caustic soda is added. The solution is heated until it turns yellow. After cooling, the addition of a few drops of dilute copper-sulphate solution should give a reddish color.

Mucin (NUCLEO-ALBUMIN).—Mucin is present in small amount in every normal urine, being more abundant in the urine of females, chiefly from the vaginal secretion. It is derived from the epithelia of the genito-urinary organs, and is considerably increased in inflammations of these organs, more especially those of the bladder, the urethra, prostate gland, and vagina. When present in large amount, the urine appears cloudy soon after it is voided, and it may form a ropy, jelly-like mass, which sinks to the bottom of the vessel.

To detect its presence in urine, dilute with two or three times the amount of water to prevent a precipitation of uric acid upon addition of acid. After dilution add an excess of acetic acid. If mucin is present, a more or less pronounced precipitate forms. The precipitate may be purified by dissolving in water with a small amount of caustic soda, and reprecipitated by acetic acid. To detect it in urine containing considerable albumin, precipitate the albumin by boiling, and test again with acetic acid. Even small amounts can be readily detected with the microscope.

Fibrin.—Fibrin, the coagulum from blood, lymph, and exudates, is found in the urine in greater or less amount in hemorrhages from the genito-urinary tract due to various causes, and is also seen in chylous urine. In tumors of the bladder, such as papilloma and cancer, where hemorrhages occur frequently, it is of common occurrence. It is usually present in the form of coagula when the urine is voided, or may be precipitated upon standing.

Fibrin is insoluble in water, alcohol, ether, and in salt solutions, as well as in weak acids and alkalies. The addition of weak acid solutions, such as hydrochloric acid, causes it to swell up into a gelatinous mass, which becomes soluble after prolonged boiling. The solutions give the general reactions of albumin. It is, however, much easier to detect its presence by the microscope.

Hemoglobin, the chief coloring matter of the blood, is, from a chemical standpoint, a chromoprotein. It is discussed under coloring matters.

Other protein substances, such as *histon* and *nucleo-histon*, are occasionally found in urine, but have no known clinical value.

CHAPTER VI.

CARBOHYDRATES.

A. GRAPE SUGAR.

Grape sugar, dextrose, or **glucose** ($C_6H_{12}O_6$) is the only important carbohydrate found in urine. There can be little doubt that the urine may contain small amounts of sugar under normal conditions, but the amount is so minute, usually less than 0.02 per cent, that a positive reaction is not obtained with the general methods of detecting dextrose.

The presence of grape sugar in the urine in appreciable amounts temporarily does not necessarily signify the existence of diabetes, any more than the presence of albumin signifies the existence of a nephritis. After a diet rich in carbohydrates or the ingestion of considerable quantities of sweet alcoholic beverages, sugar may appear in the urine temporarily; such a condition is spoken of as a *physiological or alimentary glycosuria.*

Pathologically, glycosuria may appear in the urine as a temporary condition (*transitory glycosuria*) in the course of a number of diseases, such as Asiatic cholera, intermittent fever, affections of the heart, lungs, liver, brain, and spinal cord; alcoholism, gout, and tumors of the pancreas. It may occur during pregnancy and in the course of acute contagious diseases, such as scarlatina. Furthermore, glycosuria may be present in poisoning with certain drugs, such as the alkaloids of opium, chloral, chloroform, amyl nitrite, caffeine, curare, and carbonic oxide; also after the use of large doses of thyroid extract.

Whenever sugar is persistently present in appreciable quantity, we always have to deal with diabetes mellitus. This disease has been observed at all ages, and large amounts of sugar may be found; 300 gm. in twenty-four hours are not rare, 100 to 200 gm. being the average; more than nine or ten per cent are, however, not often excreted. In the milder cases no sugar may be present in the morning urine; hence it is important to examine the urine at different times of day. In the severer cases it is never absent from the urine. The amount of sugar does not seem to be a criterion for the severity of the case. A large amount of pale or straw-yellow urine, even with a comparatively low specific gravity, should always be an indication to examine for sugar, even if no other clinical evidences point toward the presence of the disease.

Detection of Sugar in Urine.—The tests for sugar are numerous, and in mild cases it may be necessary to resort to two or even three different tests before we are positively able to determine the presence of sugar.

1. Moore-Heller Test.—Perhaps the simplest is the Moore-Heller test. Although by no means absolutely reliable, it is in many cases sufficient to determine the approximate amount of sugar. The method is the following: Pour into a test tube two parts of urine and one part of a ten per cent caustic-potash solution; boil the upper portion for two or three minutes. Phosphates, if precipitated in large amount, must be filtered off. When sugar is present a change of color will take place after boiling, which can be approximately estimated as follows: One per cent or less of sugar gives a canary-yellow color, the color being somewhat more intense than that of the original unmixed urine; between one and two per cent gives a wine-yellow color; between two and three per cent, a sherry color; between three and four per cent, a rum color; and above four per cent, a dark brown or even black color. By the addition of a few drops of nitric acid, the liquid loses its dark color and gives out an odor similar to molasses.

This test is only a tolerably reliable one, but in many cases will answer the purpose. The addition of caustic potash to cold urine may produce a dark color, which is due to the presence of coloring matters of the bile. The white flocculent precipitate, which is almost invariably seen with this test, is partly due to the phosphates which caustic potash may precipitate in cold urine, and partly to mucin. The presence of a large amount of mucin may give a similar reaction.

The most commonly used methods of searching for sugar in the urine are the copper tests. They all depend upon the fact that in alkaline solutions grape sugar reduces copper salts to oxide.

2. Trommer's Test.—The oldest of these tests is Trommer's, which is used in the following manner: To one or two parts of urine in a test tube add one part of caustic potash or soda, adding, drop by drop, a ten per cent solution of sulphate of copper, and shake until the mixture shows a blue color. Heat the upper part of the mixture, and if sugar is present a precipitate of yellow cuprous hydroxide will result, which at first shows plainly in the bluish liquid, but gradually spreads over the entire fluid, and a red sediment of cuprous oxide is formed.

If this reaction takes place upon heating, a similar mixture may be made and set aside for a number of hours without heating; if sugar is present in rather large quantities, a similar precipitate will form.

Should the reaction by heating be at all doubtful, the second test must always be made, since many of the other organic substances, which reduce the salts of copper, do so only after heating and boiling.

This test is open to a number of objections. Albumin, if present in large quantities, must first be removed, since it interferes with the reduction of the cupric oxide. A number of substances are, furthermore, found in urine which have the property of reducing copper oxide in an alkaline solution, among which may be mentioned uric acid, creatinin, hippuric acid, and mucin. Again, a small amount of sugar may be present in urine and fail to reduce the oxide in the presence of other substances, such as urate of ammonium, chloride of ammonium, and other ammoniacal compounds.

3. FEHLING'S TEST.—Fehling's reagent consists of two solutions, the copper solution and the alkaline solution.

(1) Copper solution: Dissolve 34.639 gm. of pure crystallized copper sulphate in a sufficient quantity of water under gentle heat, and dilute with water to 500 c.c.

(2) Alkaline solution: Dissolve 173 gm. of chemically pure crystallized potassium and sodium tartrate and 100 c.c. of caustic-soda solution, of a specific gravity of 1.120, in sufficient water to make 500 c.c.

These solutions must be kept in separate bottles in a dark place and equal volumes mixed before using. Ten cubic centimetres of this solution will be reduced completely by 0.05 gm. of sugar. Even if kept separately Fehling's solution may decompose, and will then give a precipitate on heating, without the addition of urine containing sugar.

The solution may be used by pouring a small quantity into a test tube and diluting it with two or three times the amount of water. The mixture should be boiled for a few seconds. If it remains clear after boiling, which will usually be the case when the two solutions are kept separate and are not too old, add the urine to be tested drop by drop, at the same time continuing the boiling. If sugar be present in any quantity, the first few drops will usually cause a yellow precipitate; if the addition of urine is continued, a yellowish-red sediment will soon fall to the bottom of the test tube. Should no such precipitate occur, the addition of urine may be continued until an equal volume of urine has been added; if then no yellow precipitate appears upon boiling, the urine is free from sugar.

(4) HAINES' TEST.—This is a modification of Fehling's, for which stability is claimed, if well prepared, though kept on hand indefinitely. The improved formula consists of 2 gm. (30 grains) of pure copper sulphate and 16 c.c. (one-half ounce) of distilled water; make a perfect

solution and add 16 c.c. (one-half ounce) of pure glycerin; mix thoroughly, then add 160 c.c. (5 ounces) of liquor potassæ.

In testing with this solution, pour about 4 c.c. (1 drachm) into a test tube and boil it gently. Next add six to eight drops of the urine and again boil. If sugar be present, a copious yellow or yellowish-red precipitate is formed. If no such precipitate occurs, sugar is not present.

By a modification of this test its delicacy has been increased, and the test can be performed by the ring or contact method.* "The modification enables a detection with certainty of amounts above 0.03 per cent of sugar, which is about the upper limit of the so-called normal sugar of the urine."

"Owing to the increase of the specific gravity of the solution, by the addition of a larger amount of glycerin, the employment of the contact test becomes a matter of the greatest simplicity. However, one precaution must be taken before this test may be applied. Owing to the fact that the phosphates of the urine precipitate when added to the alkaline copper solution, these interfering substances must be removed before the contact test shows in its most perfect manner, otherwise a confusing contact ring is observed, which might lead to possible errors in interpretation. This removal is accomplished by adding to the urine in a test tube 5 or 6 drops of a 5 or 10 per cent solution of sodium or potassium hydroxid and allowing the phosphates to settle out or centrifuging or filtering if desired to hasten the process." For ordinary clinical purposes this removal becomes necessary only if the amount of sugar is below 0.1 per cent; if above that amount, the reaction with the untreated urine is usually quite distinct.

The composition of the improved Haines' solution is the following: Copper sulphate, 5 gm.; glycerin, 250 c.c.; potassium hydroxid, 20 gm.; distilled water to 1000 c.c. The copper sulphate is dissolved in a mixture of the glycerin and an equal amount of water, with the aid of gentle heat. The potassium hydroxid should be dissolved in about 200 c.c. of water and added to the copper solution with constant stirring, the whole being made up to volume with distilled water. This solution keeps indefinitely.

While the solution may be used in the same manner as the original solution, a much more delicate reaction is obtained as follows: "Heat about 5 c.c. of the copper solution to boiling in a test tube, remove from the flame and hold at an angle of from 30 to 40 degrees. To this add, by means of a medicine dropper, from 10 to 20 drops of the urine freed from phosphates in such a manner that a distinct zone of contact is

* Haines, Pond and Webster: Jour. Am. Med. Assoc., Vol. 74, 1920.

formed between the copper solution and the urine. The tube is then placed in an upright position and the reaction noted. If sugar is present in quantities exceeding 0.1 per cent, a brick-red or yellowish ring will immediately appear at the junction of the two liquids. If the amount of sugar is less than 0.1 per cent, ranging down to 0.03 per cent, the ring will appear in from a few seconds to slightly less than a minute, the smaller quantities showing slower reactions with a tendency to a more yellowish color of the ring. In urines containing no pathologic sugar, no ring of any kind will be noted at the zone of contact."

5. BENEDICT'S TEST.—This is an excellent modification of the old copper tests and one of the most delicate tests known. The solution, which does not deteriorate upon long standing, has the following composition: Crystallized copper sulphate, 17.3 gm.; sodium or potassium citrate, 173 gm.; crystallized sodium carbonate, 200 gm. (or anhydrous 100); distilled water, to make 1,000 c.c. The citrate and carbonate are dissolved together (with the aid of heat) in about 700 c.c. of water. The mixture is then poured (through a filter if necessary) into a large beaker. The copper sulphate (which should be dissolved separately in about 100 c.c. of water) is then poured slowly into the first solution, with constant stirring. The mixture is then cooled and diluted to 1 litre, and may be kept indefinitely in uncolored glass- or cork-stoppered bottles.

The method is the following: To about 5 c.c. of the reagent in a test tube, add eight or ten drops, but no more, of the urine to be examined. The mixture is then boiled vigorously for at least one, but preferably two minutes, and allowed to cool spontaneously. In the presence of glucose the entire body of the solution will be filled with a precipitate, which may be red, yellow, or greenish in tinge. If the quantity of glucose be low, that is under 0.3 per cent, the precipitate forms only upon cooling. If no sugar be present, the solution either remains perfectly clear, or shows a faint turbidity that is blue in color, and consists of precipitated urates.

This reagent is about ten times as sensitive to sugar in urine as is Fehling's or Haines' solution, and unlike these latter solutions, is not appreciably reduced by creatinin, uric acid, chloroform, or the simple aldehydes. Even very small quantities of sugar (0.1 per cent) yield precipitates of considerable bulk with this reagent, and the positive reaction for glucose is the filling of the entire solution, either before or after cooling, with a precipitate, so that the mixture becomes opaque. Since bulk, and not color, of the precipitate is made the basis of a positive reaction, the test may be carried out as readily in artificial light as in daylight, even when examining for very small quantities of sugar.

Besides the copper tests, bismuth tests are also used; these depend upon the power of grape sugar to reduce the salts of bismuth, giving a black precipitate. Of these, two good tests are the following:

6. BÖTTGER'S TEST.—Pour one part of urine into a test tube and add an equal quantity of a concentrated solution of sodium hydroxide or caustic potash, and a small quantity of subnitrate of bismuth. Boil for a short time. If sugar is present, a gray or black precipitate appears, which will be deposited on the sides of the test tube. If the quantity of sugar is small, a grayish color appears. Albumin, if present in large quantities, must first be eliminated by boiling and filtration.

7. NYLANDER'S TEST.—Nylander's reagent is prepared by dissolving 4 gm. of Rochelle salt in 100 c.c. of a ten per cent. sodium or potassium hydroxide, warming the solution and adding 2 gm. of bismuth subnitrate. The reagent is then cooled and filtered; it should be kept in a dark bottle. The test is carried out as follows: To about 5 c.c. of urine in a test tube add one-tenth its volume of the reagent and heat for from three to five minutes. If sugar is present, the mixture will darken, and upon standing for a few moments a black color will appear, which is due to the precipitation of bismuth. As small an amount of glucose as 0.08 per cent may be detected by this reaction, but when traces only are present the solution will turn brown and not black. Reduction of bismuth after the fluid has cooled is not due to bismuth. When no sugar is present there may be a white precipitate due to phosphates. When more than a trace of albumin is present, this must be removed by boiling and filtering before applying the test, since a similar change of color is produced with albumin. When an excess of urinary coloring matters is present, a partial reaction may occur, and the same may occur after different medicinal substances.

8. PHENYLHYDRAZIN TEST.—Phenylhydrazin forms with dextrose a compound known as phenylglucosazon, which is almost insoluble in cold water and separates in hot solutions in a characteristic crystalline form. This test is performed as follows: Pour 10 c.c of the urine into a test tube and add to it 0.4 gm. of phenylhydrazin hydrochloride and 0.8 gm. of sodium acetate; immerse the test tube in a water bath and boil for one-half to one hour; remove the tube and set it aside to cool. At the end of half an hour typical crystals of phenylglucosazon separate when sugar is present. These crystals appear under the microscope in the form of fine, bright yellow needles, arranged in bundles, sheaves, or rosettes.

These eight tests represent only a fraction of those in use, but are the more important. The others offer no advantages over those described.

Quantitative Tests for Sugar.—For a rough quantitative determination of sugar in the urine, the Moore-Heller test, previously described, can be used. It is, however, not very accurate, and of little value if the amount of sugar is below one per cent. Of the other methods employed for quantitative estimation, the fermentation tests, Fehling's, and Benedict's tests are simple and fairly accurate. The method by means of the polariscope is probably the most accurate when the amount of sugar exceeds one per cent. It depends upon the fact that dextrose rotates polarized light toward the right, and that the degree of rotation varies in proportion to the percentage of sugar in the urine. The different instruments devised for this purpose are elaborate and costly.

FEHLING'S TEST.—The principle upon which Fehling's solution depends lies in the fact that, in the reduction of oxide of copper by grape sugar, the blue color disappears by the addition of a definite quantity of the sugar. As before said, 10 c.c. of the solution correspond to 0.05 gm. of sugar. The test may be conducted in the following manner: Dilute 1 c.c. of Fehling's solution with 4 c.c. of water in a test tube, and, after heating, add 0.1 c.c. of the urine to be examined from a graduated pipette. Heat must then be reapplied, the precipitate watched, another 0.1 c.c. added, and the heat again applied, until, after allowing it to stand for a short time, it is found that all the blue color is removed from the solution. If, in doing this, 1 c.c. of urine has been added, it contains one-half of one per cent of sugar; if more than 1 c.c., it contains less than one-half per cent, but more than one-fourth per cent; if 2 c.c. are used, it contains one-fourth per cent; and if 0.5 c.c. is used, it contains one per cent of sugar. If the proportion of sugar is large, as is usually the case with a high specific gravity, the urine should be diluted five to ten times.

ROBERTS' FERMENTATION TEST.—This is an excellent and simple test, being used as follows: Into each of two bottles, one of four ounces, the other of twelve ounces capacity, pour 4 ounces of urine. Add a piece of fresh yeast the size of a walnut to the urine in the larger bottle, which must be closed with a cork nicked for the escape of gas evolved by fermentation. The smaller bottle must be tightly corked, and the two bottles placed side by side in a uniform temperature of 68° to 75° F.—the average temperature of the room. At the end of twenty-four hours fermentation will be completed. The specific gravity of each specimen must then be carefully taken by means of the urinometer, and the difference of the specific gravity indicates the number of grains of sugar per fluidounce. For example, if the specific gravity of the unfermented urine is 1.035 and that of the fermented urine 1.020, the urine contains 15 grains of sugar to the fluidounce, or three per cent. This test, although not absolutely accurate, is sufficiently so for practical purposes.

Einhorn's Fermentation Saccharometer.—One of the simplest tests, which will be found to answer all purposes, is by means of Einhorn's fermentation saccharometer (see Fig. 14). The apparatus is put up in the form of a set, consisting of two saccharometers and one graduated test tube. The method is the following: Take 1 gm. (about 15 grains) of fresh commercial compressed yeast, and shake thoroughly in the graduated test tube with 10 c.c. of the urine to be examined. Then pour the mixture into the bulb of the saccharometer. By inclining the apparatus the mixture will easily flow into the cylinder, thereby forcing out the air. Owing to the atmospheric pressure, the fluid does not flow back, but remains there. Leave the apparatus undisturbed for twenty or twenty-four hours in a room of ordinary temperature.

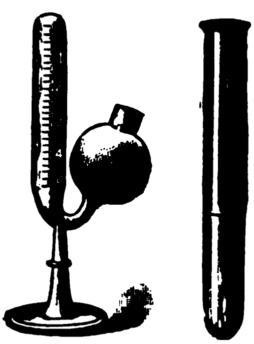

Fig. 14.—Einhorn's Fermentation Saccharometer.

If the urine contains sugar, the alcoholic fermentation begins in about twenty to thirty minutes. The evolved carbonic-acid gas gathers on the top of the cylinder, forcing the fluid back into the bulb. On the following day the upper part of the cylinder will be found filled with carbonic-acid gas. The changed level of the fluid in the cylinder shows that the sugar reaction has taken place, and indicates, by the numbers upon the cylinder to which it corresponds, the approximate amount of sugar present. If the urine contains more than one per cent of sugar, it must be diluted with water before being tested; urine of a specific gravity of 1.018 to 1.020 may be diluted twice; of 1.021 to 1.028, five times; 1.029 to 1.038, ten times.

In carrying out this test it is always advisable to take, besides the urine to be tested, a normal specimen, and make the same fermentation test with it. The mixture of the normal urine with yeast will, on the following day, have only a small bubble on the top of the cylinder. This proves at once the efficacy and purity of the yeast. If, in the suspected urine, there is also a small bubble on the top of the cylinder, no sugar is present; but if there is a much larger gas volume, we are sure that the urine contains sugar.

Benedict's Quantitative Test.—By modifying his solution for qualitative sugar tests, Benedict has been able to apply the reagent to a rapid and accurate estimation of sugar in the urine. "Like Fehling's quantitative process, the method is based on the fact that in alkaline solution a given quantity of glucose reduces a definite amount of copper, thus decolorizing a certain amount of the copper solution. The copper is, however, precipitated as cuprous sulphocyanate, a snow-white compound, which is an aid to accurate observation of the disappearance of the last trace of blue color. The solution for quantitative work, which keeps indefinitely, has the following composition: Pure crystallized copper sulphate, 18 gm.; crystallized sodium carbonate, 200 gm. (or anhydrous 100); sodium or potassium citrate, 200 gm.; potassium sulphocyanate, 125 gm.; five per cent potassium ferrocyanide solution, 5 c.c.; distilled water to make a total volume of 1000 c.c. With the aid of heat dissolve the carbonate, citrate and sulphocyanate in enough water to make about 800 c.c. of the mixture, and filter if necessary. Dissolve the copper sulphate separately in about 100 c.c. of water, and pour the solution into the other liquid, with constant stirring. Add the ferrocyanide solution, cool and dilute to exactly one litre. Of the various constituents, the copper salt only, need be weighed with exactness. Twenty-five cubic centimetres of the reagent are reduced by 50 mgm. (0.050 gm.) of glucose."

The sugar estimation is conducted as follows: "The urine, 10 c.c. of which should be diluted with water to 100 c.c. (unless the sugar content is believed to be low), is poured into a 50 c.c. burette up to the zero mark. Twenty-five cubic centimetres of the reagent are measured with a pipette into a porcelain evaporation dish (25–30 cm. in diameter), 10 to 20 gm. of crystallized sodium carbonate (or one-half the weight of the anhydrous salt) are added, together with a small quantity of powdered pumice stone or talcum, and the mixture heated to boiling over a free flame until the carbonate has entirely dissolved. The diluted urine is now run in from the burette, rather rapidly until a chalk-white precipitate forms, and the blue color of the mixture begins to lessen perceptibly, after which the solution from the burette must be run in a few drops at a time, until the disappearance of the last trace of blue color which marks the end-point. The solution must be kept vigorously boiling throughout the entire titration. If the mixture becomes too concentrated during the process, water may be added from time to time to replace the volume lost by evaporation."

"The calculation of the percentage of sugar in the original sample of urine is very simple. The 25 c.c. of copper solution are reduced by exactly 50 mgm. of glucose. Therefore the volume run out of the burette to effect the reduction contained 50 mgm. of the sugar. When the urine is diluted 1:10, as in the usual titration of diabetic urines, the formula for calculating the per cent of the sugar is the following: $\frac{0.050}{x} \times 1000$ = per cent in original sample, wherein x is the number of cubic centimetres of the diluted urine required to reduce 25 c.c. of the copper solution."

"In the use of this method chloroform must not be present during the titration. If used as a preservative in the urine it may be removed by boiling a sample for a few minutes, and then diluting to the original volume."

Benedict claims great accuracy for this method, it being, as he says, probably more exact than any other titration method available for sugar work.

B. OTHER CARBOHYDRATES.

Fruit sugar, levulose ($C_6H_{12}O_6$), is rarely found in urine, and may be associated with dextrose in diabetes. It has been found in cases of melancholia and impotence, but its exact clinical significance is not understood. Levulose rotates polarized light to the left, in contradistinction to dextrose, which rotates it to the right. It reduces salts of copper, but more feebly than dextrose.

Levulose gives a typical reaction, known as *Seliwanoff's reaction:* To 10 c.c. of urine add a small amount of resorcin and 2 c.c. diluted hydrochloric acid; mix and heat in a test tube. If levulose is present the liquid turns red and precipitates a dark sediment, which is soluble in alcohol with a bright red color.

Milk sugar, lactose ($C_{12}H_{22}O_{11}$), is sometimes found in the urine of nursing women, but is usually present in small amount only, rarely more than one per cent. Pavy has found it as late as five months after parturition in women in whom an overabundance of milk secretion was present, as well as in some women who interrupted the nursing of their children. It has no pathological significance, but is important because it may be mistaken for dextrose

Lactose may be detected with *Rubner's test:* To 10 c.c. of urine add 3 gm. of lead acetate; filter off the precipitate and heat the filtrate in a test tube for a few minutes, until a yellowish-brown color appears; now add ammonia and continue heating. If lactose is present, a brick-red color appears in the solution and a cherry-red or copper-colored precipitate settles at the bottom of the test tube, while the supernatent fluid becomes colorless.

Maltose or **isomaltose** ($C_{12}H_{22}O_{11}$) has been found in a number of cases of disease of the pancreas in very small amount, usually not more than 0.1 to 0.5 per cent. It reduces copper solutions, but not as strongly as does glucose. Ten cubic centimetres of Fehling's solution are completely reduced by 0.0807 gm. of maltose.

Cane sugar, saccharose ($C_{12}H_{22}O_{11}$) is rarely found in urine and is of no clinical importance. It may be found after eating large amounts of cane sugar, and in the urines of hysterical patients who have added it to deceive the physician. Pure saccharose does not reduce Fehling's solution.

Pentoses ($C_5H_{10}O_5$) are occasionally found in urine; the more important are rhamnose, arabinose and xylose. Different varieties of pentosuria have been described: 1 Alimentary pentosuria, which is found after the ingestion of pentose-containing food, such as apples, plums, cherries and different vegetables, also after drinking fruit syrups and malt liquors; 2. diabetic pentosuria, pentose being present in severe forms of diabetes; 3. idiopathic or intrinsic pentosuria, the cause of which is unknown.

The pentoses reduce copper solutions, but the reduction is much slower than with other carbohydrates, appearing during the cooling of the fluid. Ten cubic centimetres of Fehling's solution are reduced by 0.0542 gm. of pentose. The fermentation test is negative. With Nylander's test they give a gray precipitate. They may be detected with *Bial's orcin test.* The reagent consists of 500 c.c. of thirty per cent hydrochloric acid, 1 gm. of orcin, and twenty-five drops of ten per cent ferric chloride solution. Five cubic centimetres of this reagent are boiled in a test tube and after removal from the flame the urine is added drop by drop, at most 1 c.c. being used; a green color will appear almost immediately.

Glycuronic acid ($C_6H_{10}O_7$) does not occur in the urine as such, but only in combination with different aromatic substances of the urine. It has little, if any clinical significance, but may be mistaken for glucose. It is increased after the administration of chloral, naphthol, phenol, menthol, camphor, oil of turpentine, morphine, antipyrine, and other substances. It reacts to the reduction tests with copper and forms a crystalline compound with phenylhydrazin, but does not ferment with yeast. It is difficult to differentiate it from the pentoses. Glycuronic acid itself is dextrorotatory, but its paired combinations, which exist in normal urine, are levorotatory.

Cammidge's Reaction.—A number of years ago Cammidge described a reaction, which he observed in the urines of persons suffering from diseases of the pancreas, and regarded by him as useful in the diagnosis of pancreatic diseases. The test depends upon the production of characteristic osazone crystals when the urine is treated with phenylhydrazin after boiling with hydrochloric acid. It is not as yet definitely settled what substance produces the reaction, but it is apparently some carbohydrate-like, possibly some dextrine-like substance.

Cammidge claimed that his reaction is positive in all cases of pancreatic diseases, but in no other diseases. Later researches, however, have proven that, although the reaction is given in some cases of acute and chronic pancreatitis, as well as in tumors of the pancreas, it is not pathognomic, may occur in other conditions, and may not even be present in pancreatic diseases.

The urine to be examined should be from a mixed twenty-four hours' specimen, and must be free from albumin and glucose; if these substances are present they must first be removed. The test can best be carried out in the following manner: To 40 c.c. of clear, filtered urine in a small flask add 2 c.c. of strong hydrochloric acid, boil for ten minutes, cool, and add enough distilled water to make 40 c.c. Neutralize the excess of acid by adding slowly 8 gm. of powdered lead carbonate, allow the mixture to stand for a few minutes, then cool and filter. To the filtrate add 8 gm. of powdered tribasic lead acetate, filter again, and treat with 4 gm. of powdered sodium sulphate; heat to the boiling point and allow to cool. Remove the lead sulphate by filtration. Ten cubic centimetres of the clear filtrate are made up to 17 or 20 c.c. with distilled water, 0.8 gm. of phenylhydrazin hydrochlorate, 2 gm. of sodium acetate, and 1 c.c. of a fifty per cent acetic acid are added, and the mixture again boiled for ten minutes. Filter while hot, and make the filtrate up to 15 c.c. with warm water. When the mixture has cooled, a light yellow, flocculent precipitate forms, which under the microscope, will be found to consist of yellow crystals arranged in sheaves and rosettes. These crystals dissolve within a few minutes when treated with a thirty-three per cent solution of sulphuric acid.

This test, when positive, can at best be looked upon as a confirmatory sign in cases in which the clinical symptoms strongly point to pancreatic disease. It has no negative value.

CHAPTER VII.

OTHER ABNORMAL CONSTITUENTS.

Acetone Bodies.—The term acetone bodies is applied to a group of substances, the chemical relation between which is very close; these substances are acetone, diacetic acid and β-oxybutyric acid. For a long time β-oxybutyric acid was held to be the mother-substance of the group, but it is now believed that diacetic acid is first formed and that the others are derived from it. Formerly these substances were supposed to be derived from proteins, but the present opinion is that their chief source lies in abnormal katabolism of fats. The presence of the acetone bodies in the urine, except of acetone alone in small amounts, is known as *acidosis* or *acid-intoxication*. In mild cases acetone, in more than small amount, occurs alone; in severer cases diacetic acid is also present, and in the most marked cases β-oxybutyric acid is found with or without the others.

The excretion of acetone bodies is especially observed in the severer cases of diabetes and in toxic or pernicious vomiting of pregnancy, as well as after death of the fœtus in utero; also in different febrile conditions, some malignant tumors, digestive disturbances, lesions of the central nervous system, in starvation, after chloroform narcosis, as well as in intoxication with various substances, such as phosphorus.

The simpler tests for the acetone bodies are given below under the individual substances of this group. Two tests, however, can be described here which are of advantage in different conditions. *Fittipaldi* has described an improved nitro-prusside test, which is simple and shows up diacetic acid as well as acetone; it takes but little time and the color reaction is durable. It is carried out as follows: To 4 or 5 c.c. of urine in a test tube add 0.02 gm. of finely pulverized sodium nitro-prusside; mix until the salt is entirely dissolved and then superpose 1 c.c. of ammonia on the urine, pouring it along the wall of the tube. Leave the mixture undisturbed for fifteen minutes. At the end of this time a colored zone is present between the two fluids. If this zone is a yellow to chestnut color, the acetone content is within normal range. If the zone is of a more or less deep chestnut color, there is a slight excess of acetone but no diaceturia. If the zone is violet, there is considerable acidosis. In this case the fluid is mixed, and acetic acid added drop by drop, until the fluid is slightly acid. If the reddish-purple tint throughout the whole disappears as the acid is added, more or less pronounced acetonuria is present, but without diaceturia. If, on the other hand, the purple blends into a durable ruby red, there is diaceturia and, as a rule, also pronounced acetonuria.

*Clifford Mitchell** has devised a test which can be recommended in the acidosis of diabetes mellitus and in that of the pernicious vomiting of pregnancy. The foundation of the test rests upon the fact that urine has the property of decolorizing iodine in aqueous solution, such as Lugol's iodine-potassium iodide solution. Mitchell found "that the urine of diabetic coma, and of the pernicious vomiting of pregnancy, had a greater decolorizing power, as far as iodine is concerned than that of other conditions. In other words, the urine in the acidosis of diabetes and of pregnancy contains a substance which is particularly well able to destroy the yellow color of iodine." The best way to apply the test is the following: To 145 c.c. of water add 3 c.c. of Lugol's solution and 2 c.c. of a saturated solution of picric acid, mixing thoroughly. The result is a fine clear reddish liquid of bright color. Pour this liquid into a white porcelain dish and heat it on the water bath to a temperature of about 80° C., or if a water bath is not available, over the flame until fumes are abundantly given off, boiling being avoided by turning down the flame sufficiently. The urine is now added quickly from a graduated burette or a small glass graduate, but in small amounts at a time. In acidosis the amount of urine needed to turn the bright red color to a bright yellow color is small and the smaller the worse the case. In severe cases 2 or 3 c.c. of urine will cause the red color to disappear almost immediately, while in cases of moderate severity 8 or 10 c.c. may be required. Normal urines do not usually affect the color in smaller amounts than 15 c.c. except possibly in highly concentrated specimens, when only a few hundred c.c. of urine are voided in twenty-four hours. In most cases of normal urines, having a specific gravity of between 1,015 and 1,020, the amount of urine required to effect the change from red to yellow is around 20 c.c. or considerably higher.

There is no trouble about the end reaction, as the mixture remains fairly clear, sometimes entirely clear. If the change from red to yellow is not easily recognized, it will aid to have at hand in another white dish about 150 c.c. of a saturated picric acid solution for comparison. If from day to day the color is discharged by less and less

* Clifford Mitchell: A Simple Urine Test for Acidosis. Medical Record, Vol. 95, 1919.

urine, the case is growing worse, but if more and more urine is required to turn the red to yellow, the patient is improving.

Acetone.—Acetone (C_3H_6O) is found in minute amount in normal urine (0.01 gm. in twenty-four hours), but is considerably increased in many different pathological conditions. Uutil recently it was supposed to be a decomposition product of proteins, but it is now believed to be formed chiefly from the breaking down of fatty tissues or fatty foods within the organism.

The most important pathological condition in which acetone is found is diabetes (*diabetic acetonuria*). In the milder cases of the disease it is not increased, but in the severer case of diabetes the amount of acetone excreted is usually large, and it is frequently associated with diacetic and β-oxybutyric acids. Acetone in varying amounts is also present in the urine in different febrile conditions, in pneumonia, typhoid fever, scarlatina, variola, in some malignant tumors, in derangements of digestion, in mental diseases, after chloroform narcosis, in starvation, and after poisoning with many different toxic substances. Urine containing a large amount of acetone has a peculiar, sweet, wine or fruity odor.

The simplest method of detection is with *Legal's test:* Prepare a fresh, strong solution of sodium nitro-prusside by dissolving a few fragments in a little water in a test tube. To a few cubic centimetres of the urine add enough liquor sodæ or liquor potassæ to secure a distinct alkaline reaction, and to this add a few drops of the nitro-prusside solution, when a red color at once appears from creatinin. This color changes slowly to straw-yellow, but if acetone is present the addition of a few drops of concentrated acetic acid produces a purple or violet-red; if no acetone is present, the latter change does not occur. This test is not distinctive for acetone, as the reaction is also given by alcohol, by acetic aldehyde and by diacetic acid.

Jackson-Taylor modified this test as follows: To a small amount of urine in a test tube add a few drops or even an equal amount of a freshly prepared sodium nitro-prusside solution. Layer this mixture with concentrated ammonium hydrate by pouring it along the side of the tube. When acetone is present a magenta color or ring is produced at the point of contact. In the absence of acetone there will be no ring, or only a faint orange-red color.

A similar modification is that of *Lange:* To a few cubic centimetres of urine add 0.5 c.c. of glacial acetic acid and a few drops of a freshly prepared aqueous solution of nitro-prusside. Mix thoroughly and overlay the mixture with 2 c.c. of ammonium hydrate. At the point of contact a purplish-red ring is observed in the presence of acetone.

Another test is *Lieben's iodoform test,* which is best applied to the distillate of the urine; 200 or 300 c.c. of the urine, after the addition of a small amount of phosphoric or hydrochloric acid in the proportion of 3 c.c. to 100 c.c., must be distilled and the tests performed with the first 10 or 15 c.c. of distillate. To the distillate add a few drops of strong potassium-hydroxide solution and a few drops of an iodine and potassium-iodide solution. If acetone is present, a yellow precipitate of iodoform develops at once, which can be easily identified by its characteristic odor and by the appearance of characteristic thin, yellow hexagonal plates or star-like groups under the microscope. The same reaction is given by other substances which may occur in urine, notably alcohol, but more slowly.

This test has been modified by GUNNING to prevent confusion with alcohol. He adds an excess of an alcoholic iodine solution and some ammonia to the distillate or the urine itself, and if acetone is present iodoform is deposited. At first the liquid often turns black from the precipitation of nitrogen iodide, but as the precipitate settles and disappears, the yellow iodoform deposit can easily be recognized. The mixture must not be warmed as long as it contains nitrogen iodide, this being a dangerous explosive.

FROMMER'S TEST.—To 10 c.c. of urine in a test tube add 1 gm. of potassium hydrate in the solid state, and, without waiting for a complete solution, treat the mixture with 10 to 12 drops of a ten per cent alcoholic solution of salicyl aldehyde; now warm to 70° C. If acetone is present an intense purplish-red ring appears at the point of contact of the two substances. This test is very delicate and the reaction does not occur with diacetic acid, as is the case with some of the other tests.

Diacetic Acid.—The presence of diacetic or aceto-acetic acid ($C_4H_6O_3$) in the urine is usually of grave significance. It is rarely, if ever, found in urine free from acetone. Diacetic acid is found in advanced stages of diabetes, in severe fevers, malignant scarlatina, diphtheria, and measles, in cancer of the stomach and intestines, as well as in some nervous disturbances.

Diacetic acid decomposes rapidly and is converted into acetone and carbon dioxide, hence the tests for it should be carried out with perfectly fresh urine.

The simplest test is *Gerhardt's ferric-chloride reaction.* To fresh urine carefully add a few drops of a ten per cent watery solution of ferric chloride. The first few drops produce a yellowish precipitate of ferric phosphate, and the addition of the reagent is continued until all the phosphates are removed; if diacetic acid is present, the addition of a few more drops of ferric chloride will produce a typical Bordeaux-red color. If the amount of diacetic acid is small, the phosphate precipitate should be filtered off and ferric chloride added to the filtrate. The red color disappears on boiling for two minutes; this is due to the instability of diacetic acid, and at once differentiates the latter from other substances, such as salicylic acid, antipyrin acetates, and carbolic acid, which give a similar reaction, but which does not disappear on boiling.

When there is any doubt concerning the nature of the reaction, some of the urine should be acidulated with sulphuric acid and shaken up with ether. The ether is removed with a pipette and shaken up with very dilute ferric-chloride solution; if diacetic acid is present, a violet color results, which changes to a Bordeaux-red upon further addition of ferric chloride. The presence of as small an amount of diacetic acid as 0.01 per cent still gives this reaction.

Another good test, which in some cases is even to be preferred to Gerhardt's, even though it is not as simple, is that of *Arnold* modified by *Lipliawski.* Two reagents are employed: first, a solution consisting of 1 gm. of para-amido-aceto-phenone, 100 c.c. of distilled water, and 2 c.c. of concentrated hydrochloric acid; second, a 1 per cent solution of potassium nitrite. To 6 c.c. of the first solution and 3 c.c. of the second add an equal volume of urine and one drop of concentrated ammonia; shake the mixture until it assumes a brick-red color. From 10 drops to 2 c.c. of this mixture, according to the probable amount of diacetic acid present, are treated with 15 to 20 c.c. of concentrated hydrochloric acid, 3 c.c. of chloroform and 2 to 4 drops of an aqueous solution of ferric chloride. The tube is then closed with a cork and gently shaken for one-half to one minute. When diacetic acid, even if only a trace, is present, the chloroform assumes a characteristic violet tinge; in its absence the color is yellow or light red. The violet persists for a long time. If the urine is highly colored, it is advisable to first filter it through animal charcoal. Salicylic acid, antipyrin, carbolic acid and other substances which may interfere with Gerhardt's test, do not disturb this reaction. Acetone does not give a positive reaction except when it is present to the extent of more than 1 per cent, and β-oxybutyric acid does not react at all.

β-Oxybutyric Acid.—This acid ($C_4H_8O_3$), with acetone and diacetic acid, constitutes the acetone bodies; it is always associated with diacetic acid in the urine. It is present in advanced cases of diabetes, but has also been found in scarlet fever, diphtheria, measles, scurvy, and other diseases. Chemically the correct term for this acid is β-Hydroxybutyric acid.

It may be detected by the method of *Hart,* which is the following:

To 20 c.c. of urine add an equal amount of water and a few drops of acetic acid. Boil until the volume is reduced to about 10 c.c., to remove acetone and diacetic acid, then add sufficient water to bring the amount to 20 c.c. and place 10 c.c. into each of two test tubes. To one of these add 1 c.c. of hydrogen peroxide, warm gently and allow to cool. Now apply Lange's modification of Legal's test for acetone to both tubes, and allow them to stand for a few hours. The tube which contains the hydrogen peroxide will then show a distinct red zone, while no reaction is seen in the other tube.

Indican.—Indican, or indoxyl potassium sulphate ($C_8H_6NO.SO_3K$), is derived from indol, a product of intestinal putrefaction of albuminous substances. The indol is absorbed by the blood and oxidized in the tissues to indoxyl, which combines with potassium sulphate and is eliminated in the urine. Indigo blue is formed by the oxidation of indoxyl potassium sulphate.

Indican is present in minute amount in every normal urine, about 0.015 gm. being voided in twenty-four hours with a mixed diet; the amount is increased up to 0.06 gm. by a meat diet. In many pathological conditions it may be considerably increased, and such an *indicanuria* is especially pronounced in all diseases in which increased albuminous putrefaction in the small intestine occurs. It is found in all gastro-intestinal disturbances, especially obstruction in the small intestine, in cholera, typhoid fever, tuberculosis of the intestines, peritonitis, cancer of the stomach, liver, and intestines, as well as in many other diseases.

Its detection by *Jaffe's method* is the following: Pour into a test tube a small quantity of urine and mix with an equal amount of strong hydrochloric acid; add ten or fifteen drops of chloroform and, drop by drop, a moderately strong fresh solution of chloride of lime, shaking after each drop. The chloroform readily dissolves the freshly formed indigo, and a blue color appears, which is more or less pronounced, according to the amount of indican present. Instead of chloride of lime (calcium hypochlorite) a 0.5 per cent solution of permanganate of potash, kept in a dark bottle, may be used. The chloroform may be added after the chloride of lime or permanganate of potash. Five drops of the latter to 10 c.c. of urine are sufficient.

Another good test is that of *Obermayer:* Precipitate 20 c.c. of urine with 5 to 10 c.c. of a ten per cent lead-acetate solution and filter; add an equal volume of fuming hydrochloric acid containing 2 gm. of ferric chloride to 1 litre of HCl; shake thoroughly and add 5 c.c. of chloroform; again shake. This extracts the indigo, and the blue chloroform solution settles at the bottom of the test tube. With normal urine a faint blue color results, while an increase of indican gives a dark blue color.

This test can be simplified in the following manner: Have on hand Obermayer's reagent which consists of a 0.2 per cent solution of dry ferric chloride in concentrated hydrochloric acid (ferric chloride 1.0 gm., HCl, 500 c.c.) and keeps indefinitely. To 5 c.c. of urine add an equal amount of this reagent and 10 to 15 drops of chloroform; shake thoroughly. The chloroform becomes blue in proportion to the indican present; the color increases upon standing. The test is a more reliable one than Jaffe's method. Instead of using Obermayer's reagent as such, the urine may be mixed with an equal amount of strong hydrochloric acid in a test tube, and 1 or 2 drops of a ten per cent solution of ferric chloride then added to the mixture. The amount of chloroform to be used remains the same. If the urine is quite dark in color or if bile pigment is present, the pigments may be removed by adding a solution of lead subacetate and filtering.

When potassium iodide has been taken internally, the chloroform becomes reddish or red instead of blue, due to the liberation of free iodine, the intensity of the red color varying with the amount of indican. When thymol has been added to the urine as a preservative, the color is violet. When formalin has been used as a preservative, indican cannot be detected by these methods.

A more sensitive test for indican than either Jaffe's or Obermayer's is that of *Jolles:* To 10 c.c. of urine add 2 c.c. of a twenty per cent lead acetate solution, shake and filter. To the filtrate add 0.5 c.c. of a ten per cent alcoholic solution of thymol, 10 c.c. of Obermayer's reagent and 4 c.c. of chloroform; mix thoroughly. In the presence of even minute traces of indican, the chloroform is colored a pronounced violet.

Skatoxyl potassium sulphate ($C_9H_8NO.SO_3K$) is formed in varying amount from skatol, which like indol is a product of intestinal putrefaction of protein substances. As a rule this pigment is present in smaller quantities than the indoxyl potassium sulphate, but occasionally appears in the urine in excess of the indican, and then the chloroform assumes a distinct red color instead of a blue. Clinically the substance is of little interest, and is known as indigo-red, skatoxyl-red or uro-rubin.

Ehrlich's Diazo Reaction.—The diazo reaction was suggested by Ehrlich as a valuable adjuvant in the diagnosis of typhoid fever. The nature of the substance upon which the reaction depends is uncertain. Some claim that a positive reaction indicates an abnormal decomposition of protein material, while others suppose it to be due to an increased excretion of alloxyproteic and other acids. It is not characteristic for typhoid fever, and is frequently enough absent in even pronounced cases of the disease; when present, it usually disappears at the end of the third week, but may reappear in a relapse.

The solutions necessary for the reaction are two:

1. Diazo reagent:	
Sulphanilic acid	0.25 to 1.25 gm.
Hydrochloric acid, concentrated	12.5 c.c.
Distilled water	250.0 c.c.
2. Sodium nitrite	0.1 gm.
Distilled water	20.0 c.c.

These solutions keep best in dark bottles and must be kept separately. When needed, mix 50 c.c. of the diazo reagent with 1 c.c. of the sodium-nitrite solution.

The test is performed by mixing 10 c.c. of the urine with 10 c.c. of the mixed reagents, quickly adding 2 c.c. of a ten per cent ammonia solution. If the reaction is positive the solution assumes a carmine- or deep cherry-red color, which also appears in the foam. A coffee-brown color is not indicative of a positive reaction. On standing for twenty-four hours a dark green precipitate is formed when the reaction is positive.

The diazo reaction has also been found in measles, pneumonia, scarlet fever, erysipelas, typhus, puerperal septicæmia, syphilis, cancer, and especially tuberculosis; in the latter disease the presence of the reaction is frequently an unfavorable sign, as it has been often found in cases with a rapidly fatal termination.

Different drugs, such as opium, morphine, chrysarobin, naphthalin, and heroin, when taken internally give the diazo reaction, though here a green precipitate does not, as a rule, occur on standing for twenty-four hours. Other drugs, such as tannin, creosote, guaiacol, and salol, render the diazo reaction in urine negative—a point to be remembered in tuberculosis, where a number of these drugs are frequently given.

Coloring Matters.—*Bile Pigments.*—When biliary coloring matters appear in the urine, the urine always has an abnormal color—dark yellow, brown, or greenish—and a yellow or yellowish-green froth or foam is produced by shaking. In fresh urine bilirubin is usually found in combination with alkalies; if allowed to stand exposed to the air, bilirubin becomes oxidized to the green biliverdin, as well as to the less important oxidation products, biliprasin, bilifuscin, bilihumin, bilicyanin, and choletelin. When a considerable amount of the pigment is present in the urine, the morphological elements of the sediment often have a more or less pronounced yellow or brownish color.

Bile pigments are met with in the urine in all cases in which there is an obstruction to the outflow of bile from the liver, and are seen in numerous pathological conditions of the liver, with or without the presence of jaundice. They may, furthermore, appear as a result of blood changes and after hemorrhage into the tissues. The condition is known as *choluria.*

The presence of biliary pigments in the urine can frequently be detected by the color of the urine and the foam, as well as by the yellow appearance of the elements in the sediment under the microscope. One of the best methods for detecting bile pigments in the urine is by *Gmelin's test,* which consists in placing a small quantity of strong nitric acid, containing a little yellow nitrous acid, into a test tube and gently floating a similar amount of urine upon it. If biliary coloring matters are present, a set of concentric colored rings will appear at the point of union between the acid and the urine; these rings, from above downward, will be green, blue, violet, red, and yellow, the green being the most predominant, and is indispensable in proving the presence of bile, the others being sometimes more or less indistinct and even entirely absent. A moderate amount of albumin has no influence upon this reaction.

A modification of this test by *Rosenbach* is also good: The urine is filtered through pure white filtering paper, and, after filtration, a drop of the acid is applied to the inside of the filter; around the nitric acid the same concentric rings will be observed.

Another simple test is *Ultzmann's:* To 10 c.c. of urine add 3 or 4 c.c. of a twenty-five per cent caustic-potash solution and an excess of pure hydrochloric acid. If bile pigments are present, the mixture assumes a beautiful green color.

Besides bile pigments, *bile acids* may be found in the urine with the pigments in pathological conditions of the liver. Their occurrence, however, is rare and their detection of no clinical value.

Coloring Matter of Blood.—Hæmoglobin, the chief coloring matter of the blood, may be found in the urine, either enclosed in the red blood globules, in cases of hæmaturia, or in rare instances dissolved in the urine, the affection being called hæmoglobinuria. When a small amount of blood is present in the urine, the color of the urine is not necessarily changed, and a slight cloudiness alone may or may not be found; when a large amount of blood is present, however, the color of the urine, as well as that of the sediment, is brown, reddish-brown, or red.

Hæmaturia is common, may be due to many different causes, such as severe inflammations, concretions, calculi, tumors, traumatism, tuberculosis, etc., and may occur from any portion of the genito-urinary tract. The source of the hemorrhage can be positively diagnosed only from the epithelia and other elements in the sediment under the microscope, as the macroscopic characteristics, from which it is claimed the source of the blood can be diagnosed, are in many cases entirely unreliable.

Hæmoglobinuria is due to a dissolution of the red blood corpuscles in the blood-vessels, which permits the coloring matter to escape in solution. In this condition blood corpuscles are scanty or entirely absent; when present, they are quite pale and not easily recognized. Hæmoglobinuria is occasionally found in severe infectious diseases, such as yellow fever, malignant smallpox, and scarlet fever; in extensive burns and after poisoning with different substances, such as carbolic acid, phosphorus, and naphthol. Cases of paroxysmal hæmoglobinuria also occur.

The simplest method of detecting hæmoglobin in urine is the *boiling test:* When urine is boiled and a few drops of acetic or nitric acid are added, the albuminous precipitate, always present in such cases, is not white, but has a more or less pronounced brown or brownish-red color.

HELLER'S TEST.—The earthy phosphates are precipitated from the urine by the addition of caustic potash or soda and heat; as they become precipitated they carry with them the coloring matter, and are therefore not white, but blood-red. Under the microscope the coloring matter can easily be detected whenever present in any form.

ALMENS' GUAIACUM TEST.—Thoroughly mix equal parts of tincture of guaiacum (1 part of guaiacum to 100 parts of absolute alcohol) and old oil of turpentine; upon this mixture, which must not have any blue color, layer the urine to be tested. If hæmoglobin is present, first a bluish-green and then a light or dark blue ring appears at the point of contact; on shaking, the mixture becomes blue. Urine containing many pus corpuscles also gives a blue ring with this test, which, however, disappears on heating the mixture to the boiling point.

Hæmatoporphyrin, a derivative of hæmoglobin, and *urobilin,* derived from bile and blood pigments, have been previously described.

Melanin is a dark pigment of slight clinical importance, and is only rarely found in urine; it may occur in the urine of persons suffering from melanotic sarcoma or cancer, though it is not present in all cases of this kind, and has also been observed in different wasting diseases. The urine containing melanin is not usually dark when voided, but soon becomes so upon exposure to the air; upon the addition of oxidizing agents, such as ferric chloride, sulphuric acid, or bromine, the dark color appears more rapidly and intensely. Melanin is present in the urine as a chromogen—melanogen—which becomes oxidized to melanin.

Alkapton is occasionally found in urine in different disturbances of protein metabolism and causes the urine to turn dark upon standing or the addition of an alkali. Alkaptonuria depends upon the presence of hydroquinon-acetic acid (homogentisic acid) and uroleucinic acid. The substance reduces Fehling's solution but is not affected by bismuth solutions. It is of no practical interest.

Fatty Matters.—In rare cases a varying amount of fat, rendering the urine more or less turbid, may be found. Such a condition, in which the fat is present either in a state of minute subdivision or in the form of larger oil drops, is called *lipuria* when no albumin is present, or *chyluria* when a large amount of albumin is found with an abundance of small fat globules. In both lipuria and chyluria, *cholesterin*, usually in small amount only, may be present in the urine.

The addition of ether quickly dissolves the fat, and the urine becomes clear. The microscope will reveal the presence of fat and cholesterin at once.

Leucin and *tyrosin* are products of decomposition of the albumins. They usually occur together in the urine and are mostly found in rapidly destructive processes of the liver, such as acute yellow atrophy and phosphorus-poisoning, although occasionally seen in other diseases. They can easily be detected by microscopical examination.

Cystin.—*Cystin* ($C_6H_{12}N_2O_4S_2$) occasionally appears in a number of members of the same family. It is not a normal ingredient of urine, and its chief clinical significance lies in its tendency to form calculi. Urine containing cystin may have a peculiar odor, a greenish-yellow color, and develops the odor of sulphuretted hydrogen upon standing; a grayish-white precipitate may form. When cystin is present, certain products of intestinal putrefaction, the diamins, especially cadaverin and putrescin, are almost constantly found. The neutral sulphur of the urine is greatly increased in amount in these cases of cystinuria. Cystin is soluble in ammonia and can be precipitated by acetic acid. Its microscopical appearance is quite characteristic.

PART SECOND.

MICROSCOPICAL EXAMINATION.

PART SECOND.

MICROSCOPICAL EXAMINATION.

CHAPTER VIII.

GENERAL CONSIDERATIONS.

MICROSCOPICAL examination of urine is in many cases of greater diagnostic importance than chemical examination, and should in every instance form a part of urinary analysis. To obtain a sediment, urine, before it is to be examined under the microscope, can be set aside in a well-stoppered bottle or conical vessel, preferably in a cool place, for at least

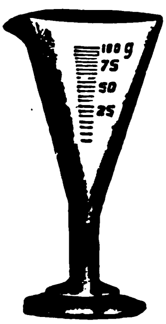

FIG. 15.—SEDIMENTATION GLASS.

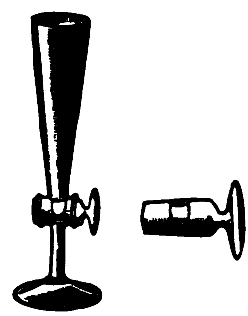

FIG. 15a.—SPAETH'S SEDIMENTATION GLASS.

six, but better twelve, hours. If a conical vessel is selected, either a plain sedimentation glass (see Fig. 15) or Spaeth's improved sedimentation glass (see Fig. 15a) may be used. The latter has a perforated stopper at the bottom, and offers advantages over the ordinary form, in that the sediment is collected in the stopper and can be removed with it. At the end of this time it will be seen that in every urine, even if perfectly normal, a sediment has appeared at the bottom of the bottle, which is to be used for microscopical examination. This sediment in normal urine will be in the form of a cloudy deposit, the *nubecula*, and consists of mucus, flat epithelia from the bladder and vagina, and a varying number of epidermal scales from the genital organs. Spermatozoa may be present in both male and female urine after sexual intercourse, and in the former after nocturnal emission. The sediment of normal urine may, furthermore, contain even a large number of salts in the early morning, when the urine is highly concentrated, while these salts may be almost entirely absent at other times.

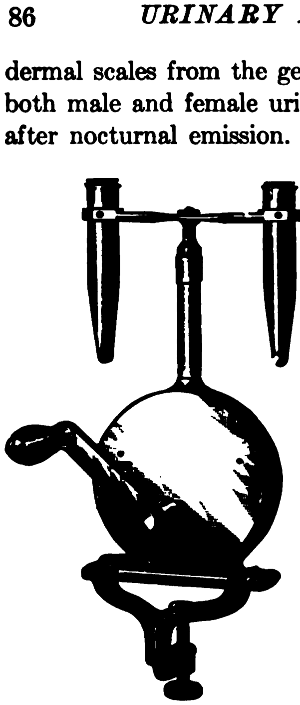

FIG. 16.—HAND CENTRIFUGE.

After standing for some time, every urine undergoes a change, the rapidity of which depends upon the temperature as well as upon the degree of the reaction when passed. An acid urine, which is perfectly clear when passed, may become turbid upon cooling, owing to the presence of a large amount of urates. Micro-organisms, especially of the class of hyphomycetes or mould fungi, and saccharomycetes or yeast fungi, may sooner or later develop, and in a small degree schizomycetes, or fission fungi. An amphoteric or even faintly alkaline urine may be clear when voided, but soon becomes more or less cloudy, the change depending partly upon the salts, but mostly upon the development of bacteria belonging to the class of fission fungi. This change takes place quickly in warm weather, and is, as a rule, more pronounced in the urine of females than in that of males, on account of the bacteria which are normally found in the vagina.

FIG. 17.—WATER-POWER CENTRIFUGE.

In pathological conditions the sediment in the urine is usually more or less increased, though in mild cases the increase is not pronounced. In severe inflammatory or suppurative processes, however, it may be very abundant, this being due to pus corpuscles, blood corpuscles, epithelia, casts, etc., which it contains. Frequently such urine is cloudy when voided, and, when an excessive amount of mucus is present, is ropy in character.

Use of Centrifuge.—To overcome the necessity of waiting for precipitation to take place and to avoid the changes due to decomposition, the *centrifuge* is considerably used. With this instrument three minutes are sufficient to obtain a proper sediment. The simplest centrifuge is operated by hand (see Fig. 16). Single-speed instruments give a speed up to 1,500 revolutions a minute; double-speed instruments, 1,000 to 4,000 revolutions. The former answers all ordinary purposes. The water-power centrifuge (see Fig. 17) is also easy to operate, giving a smooth and rapid motion; ordinary water pressure is sufficient to obtain the desired speed. Where electricity is obtainable, the electric centrifuge is the most satisfactory. The sedimentation tubes, supplied with the instrument (see Fig. 18), are either plain or graduated, and hold 15 c.c. The instrument undoubtedly has its advantages, but in some cases it is better to adhere to the old method and wait for six hours, the only precautions necessary being to keep the bottle tightly corked and in a cool place.

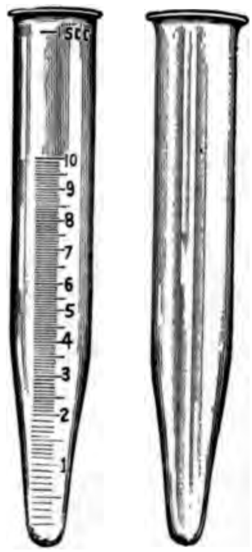

FIG. 18.—SEDIMENTATION TUBES FOR CENTRIFUGE.

One of the chief advantages of the centrifuge is that bacteria are thrown down in large numbers, so that the search for them is more successful. This is especially important in cases of suspected tuberculosis, as tubercle bacilli are found more readily in centrifugalized than in non-centrifugalized urine.

On the other hand, the great force necessary to effect sedimentation will undoubtedly change some of the minute elements to a greater or less degree. Some of the pus corpuscles may assume different shapes, irregular in character, partly due to commencing disintegration. These changes are not present in the non-centrifugalized specimen, while the number of corpuscles is the same in both. Similar changes may take place in different epithelia as well as in spermatozoa, which latter may assume peculiar forms after the use of the centrifuge. When a proper sediment is obtained by standing, the number of casts in the centrifugalized and non-centrifugalized specimens is practically the same in a given case, though here, too, some may undergo changes by centrifugalizing. Mucus-threads are more abundant and more likely to take on the form of cylindroids, and this may be quite pronounced in healthy urines, in which no pathological features are present; these cylindroids often resemble hyaline casts to such a degree as to be easily mistaken for them. Extraneous fibres, such as linen fibres, easily break into minute fibrillæ, and resemble connective-tissue shreds when the latter are not present.

When care is exercised in microscopical examination and only the perfectly distinct features are taken into consideration, the centrifuge is decidedly advantageous, but in some cases it is better to adhere to the old method of obtaining the sediment by gravity.

Mounting of Sediment.—The sediment having been obtained by either allowing at least four or six ounces of urine to stand at rest for the required time or by the use of the centrifuge, a drop of it is transferred to a slide for microscopical examination. For this purpose a glass pipette, consisting of a simple glass tube drawn to a moderately fine point at one end, may be used. This tube is passed into the urine with the upper opening closed by one finger, until it almost touches bottom, when the pressure of the finger is gently relaxed, a small amount of the sediment from different layers drawn into the tube, the latter closed again with the finger, and withdrawn. A better method is carefully to decant the upper portion of the urine, pour the sediment into a small dish, and use a camel's-hair brush to transfer a drop to the slide. Such a brush can be thoroughly cleansed with water after each examination, and is kept clean more easily than a pipette. The drop of urine is put into the centre of the slide and a cover glass slowly dropped upon it, great care being taken not to press the cover down, since even the small amount of force used may be sufficient to change the epithelia or casts. Some workers never use cover glasses, but examine the urine upon the slide without covering it. This method is uncleanly and should never be employed.

Use of Antiseptic Substances.—In order to avoid decomposition of the urine as much as possible, when it cannot be examined within twelve or twenty-four hours after being passed, large numbers of antiseptic substances, such as salicylic acid, boric acid, chloroform, thymol, formalin, and bichloride of mercury have been recommended to be added in small amount to the urine; but when not absolutely necessary, it is better to avoid them. Of these substances thymol is the best, a small crystal being sufficient. The use of formalin should be avoided, as it is apt to change a number of the ingredients of the urine. Urine kept in a cool place and in a clean bottle can be examined, even thirty-six hours after being voided, without the danger of having to deal with too many putrefactive changes. In all cases the chemical analysis should be made as soon as possible. The sediment for microscopical examination can be mixed with a little alcohol if necessary, or, still better, chromic acid.

Preservation of Sediment.—If it is desired to preserve a specimen for a variable length of time, the best method is to add from two to five drops of a five per cent chromic-acid solution to it; the only change that will take place is that the albumin becomes coagulated, appearing under the microscope in the form of irregular granular matter, irregularly scattered throughout the field. The chromic acid will preserve all the features permanently, not even causing any changes in the casts. Permanent microscopical or slide specimens are made by adding a few drops of chemically pure glycerin to a small amount of the sediment previously treated with chromic acid, until a jelly-like mass is formed, and waiting for a few days until all the superfluous water has evaporated. It is not advisable to add the glycerin to the sediment mixed with chromic acid until the watery element of the urine has become evaporated, which will be the case at the end of four or five days. If the sediment has become too thick on account of the evaporation, a little more glycerin is added, a drop then mounted upon a slide, a cover glass placed upon it, and the whole surrounded by asphalt. Specimens preserved in this manner can be kept for many years without change.

Should it be desired to preserve a large amount of the urinary sediment in a bottle, the chromic acid is added as before; but in that case it will be better to add a larger amount of a weaker solution (about one-fourth or one-half per cent). After a few weeks the upper part of the liquid is poured off and a small amount of a forty or fifty per cent solution of alcohol added, to prevent the growth of mildew. Microscopical specimens can be made years afterward from urine so preserved, by taking a drop of the sediment, mixing it with a drop of glycerin, and mounting upon a slide in the regular manner.

Another method, which preserves the elements fairly well, consists in treating the sediment with equal parts of Hayem's liquid, composed of 1 gm. of sodium chloride, 5 gm. of sodium sulphate, 0.5 gm. of corrosive sublimate, and 200 c.c. of water.

Use of Microscope and Magnifying Powers.—Every complete microscope is provided with two eyepieces or oculars, three objectives, also called lenses, a triple nose-piece and a substage with an Abbé condenser. Of the two oculars one is short (1 inch), the other long (2 inches). While these are still arbitrarily marked by some foreign makers, American makers have adopted a rational system of marking them in accordance with their initial magnification; the short eyepiece has an initial magnification of eight or ten diameters (**8x** or **10x**), the long eyepiece of four or five diameters (**4x** or **5x**). The three objectives are usually 16 mm. ($\frac{2}{3}$ inch), 4 mm. ($\frac{1}{6}$ inch), and 1.9 or 2 mm. ($\frac{1}{12}$ inch); the first two are dry objectives, the last is an oil immersion objective, also known as an homogeneous immersion objective. These objectives are attached to the nose-piece, which is of the revolving variety, so that one objective can immediately be replaced by another. The purpose of the substage condenser is to condense the light and thus give an amply illuminated field when the illumination is otherwise insufficient; this becomes necessary only when the oil immersion objective is used. The condenser should not be used with the ordinary 16 mm. and 4 mm. dry objectives, but should always be removed when working with these objectives.

The mirror below the stage for the proper illumination is plane on one side and concave on the other; the concave mirror should always be used with the dry objectives when the substage condenser has been removed, while the plane mirror is best for work with the condenser, that is, for high magnifying powers with the immersion objective. Every microscope is usually supplied with two diaphragms, one immediately below the stage, or rather on a level with the stage, the other below and in connection with the Abbé condenser. Both diaphragms may be iris diaphragms, which consist of a series of thin overlapping blades placed around a central opening, the size of which may be varied by means of a lever operating the blades. In some of the microscopes only the lower diaphragm is an iris, while the upper is of the so-called cap variety, which requires a separate piece for each aperture, and which is held by a special substage receiver. As a rule, there are three cap diaphragms, each one having an aperture of different size, which, when attached, are located immediately below and near the object. The middle sized aperture is, as a rule, the best for moderately high magnifying powers, obtained by using the 4 mm. dry objective. When the immersion objective is used, and the microscope contains two iris diaphragms, the upper iris must be opened completely, while the aperture of the lower is regulated in accordance with the amount of light required. The cap diaphragms must always be removed before the substage condenser can be adjusted.

All the complete microscopes are supplied with a rack and pinion coarse adjustment and a fine adjustment or micrometer screw. They are also provided with an inclination joint, by which the body of the microscope can be inclined to any angle between the perpendicular and horizontal. As a rule, a slight inclination of the microscope is advisable and more comfortable than an upright position of the tube.

In working with the microscope adjust the mirror so as to obtain the best light, using daylight whenever possible, but avoiding the use of direct sunlight. As to the use of artificial light, both electric light, gas light, especially a Welsbach burner, or even an ordinary oil lamp may be used. Always work with both eyes open; never close one eye. Place the slide specimen on the stage, fastening it with the clips, focus the body tube down by means of the coarse adjustment until the objective is within a short distance of the specimen; now look through the eyepiece and slowly elevate the tube with the coarse adjustment, until the specimen is brought fairly well into focus; use the fine adjustment to obtain the sharpest focus. Always keep two fingers of the left hand, preferably the thumb and index finger, on the micrometer screw, so as to constantly retain a perfectly clear focus, remembering that the fine adjustment has only a limited range and must only be turned to a slight degree in either direction. If the features in the specimen become lost to view completely, no attempt should be made to obtain a clear field again with the fine adjustment, but the coarse adjustment should be used in the manner explained above. Two fingers of the right hand should be used to move the specimen about slowly, so that its different fields are gradually brought into view. A mistake frequently made with urine specimens is that instead of focusing the object itself, the top of the cover glass is brought into focus. Minute dust particles are always present on the top of the cover glass, and these may take on the most varied appearances, frequently resembling crystals of different kinds. Such dust particles, however, always have a peculiar grayish appearance, even though their shapes and sizes vary. When not absolutely certain that the correct focus has been obtained, it is always advisable to draw the tube up with the coarse adjustment, and then repeat the process of obtaining the correct focus.

Great difficulty is frequently encountered in finding all the features present in a specimen of urine under the microscope, or in diagnosing them correctly, this being in many cases due to the want of a proper magnifying power. For the study of urine, the magnifying power should always be between 400 and 600 diameters, the average being 500; such a magnifying power is obtained by the use of a 4 mm. dry objective and a short eyepiece; the Abbé condenser should always be removed, since too much light is obtained with it and the definition of the features in urine work is much clearer without it. The general custom of examining urine specimens with low magnifying powers, about 100 diameters, using the 16 mm. objective, cannot be recommended, since the majority of the features present in urine cannot be differentiated with such a low power, and even casts cannot always be diagnosed with certainty.

Again, there are many different features as well as extraneous matters, which resemble casts with low power, but which are not tube-casts; their positive differentiation is only possible with higher magnifying powers. Under no circumstances should the study of a specimen of urine ever be attempted without the drop upon the slide first being covered by a cover glass and evenly spread out. It is absolutely impossible to obtain a satisfactory specimen without this, not to speak of the uncleanliness of such a method, and the ease with which an objective can be soiled.

When a urine specimen is to be studied for micro-organisms, smears of the centrifugalized specimen must be made, fixed and stained. Staining of a urine specimen except for bacterial examination is not only unnecessary but positively misleading. Specimens stained for micro-organisms are best examined with the oil immersion objective, and for this purpose the Abbé condenser is essential. While both tubercle bacilli and gonococci can be seen with a power of 500 or 600 diameters in a well stained specimen, their study with a magnifying power of 900 or 1000 diameters, as obtained with the oil immersion objective and the short eyepiece is far more satisfactory.

In studying a specimen under the microscope it will be found of great advantage to keep a record of all the features as they are found, and also to note their comparative numbers. Too much stress cannot be laid upon the fact that, in the study of the cellular elements, the comparative sizes of corpuscles and epithelia, especially the smaller varieties, can alone lead to correct diagnoses. Such a differentiation is only possible when magnifying powers of at least 400, but preferably 500, diameters are used.

CHAPTER IX.

CRYSTALLINE AND AMORPHOUS SEDIMENTS.

THE crystalline and amorphous or chemical sediments found in urine are mostly the different acids and salts, though a number of other unorganized sediments may also be present.

I. *ACIDS AND SALTS.*

The salts which may be found under the microscope are seen partly in acid and partly in alkaline urine, and the sediments are the following:

A. ACID SEDIMENTS.

1. Uric acid 2. Sodium urate Amorphous 3. Calcium oxalate	*Common*
4. Cystin 5. Creatinin 6. Hippuric acid 7. Leucin 8. Tyrosin 9. Calcium sulphate 10. Sodium urate Crystalline	*Rare*

B. ALKALINE SEDIMENTS.

1. Triple phosphates or ammonio-magnesian phosphates (*a*) Complete (*b*) Incomplete 2. Simple phosphates or calcium phosphates (*a*) Amorphous (*b*) Star-shaped, or stellate 3. Ammonium urate	*Common.*

4. Calcium carbonate.—*Less common.*
5. Magnesium phosphate.—*Rare.*

A. ACID SEDIMENTS.

1. URIC ACID.—Uric acid is a constant ingredient of the urine, and is frequently seen under the microscope. Its amount is greatly increased by an abundant protein diet, such as meat, especially with diminished

either in front view or edgewise, and frequently smaller crystals, sometimes quite irregular, are found within the larger ones.

Another form (see Fig. 21) is often seen in highly acid urine, and is usually found with gouty or rheumatic processes or with the formation

FIG. 21.—CRYSTALS OF URIC ACID, FROM HIGHLY ACID URINE (× 450).

of uric-acid concretions in the bladder. These crystals appear in peculiar spear, comb, and brush shapes or in exaggerated lozenges. The spear shapes are in many cases very pronounced. In persons in whom the so-called uric-acid diathesis exists, these forms are frequently seen.

Still another variety of uric acid (see Fig. 22) consists of concretions of varying sizes, irregular plates, masses, and needles, either single, double, or conglomerated in the form of stars. Occasionally dumb-bell forms are also met with. The passage of such concretions or gravel proper, when at all abundant, is almost invariably accompanied by more or less severe pain. When in larger masses, we have the uric-acid cal-

FIG. 22.—URIC-ACID CONCRETIONS (× 500).

culi or stones, which form the largest number of renal stones, being perhaps seventy per cent of all calculi passed.

Quite frequently small, irregular plates of a light or dark yellow color are seen under the microscope; the sediment in which these are found may be of a mucous or granular character, which gives no indication of containing any uric acid. Different varieties of uric acid with calcium-oxalate crystals and occasionally a varying amount of urates are not in-

2. Sodium Urate.—Sodium urate (see Fig. 24), when present in large amounts, forms the so-called clay-water sediment, which renders the urine turbid upon cooling. It may be found alone or in combination with uric acid and potassium urate, from which latter it can hardly be distinguished. Such a sediment is the so-called *sedimentum lateritium*. Sodium urate usually consists of groups of light or dark brown, fine, amorphous granules in a moss-like arrangement, which easily adhere to foreign substances as well as to mucus and epithelia. The groups vary greatly in size and are at times quite large.

This salt is of common occurrence, and is found in all slight febrile derangements, after mental and physical exertion, in colds, catarrhs of

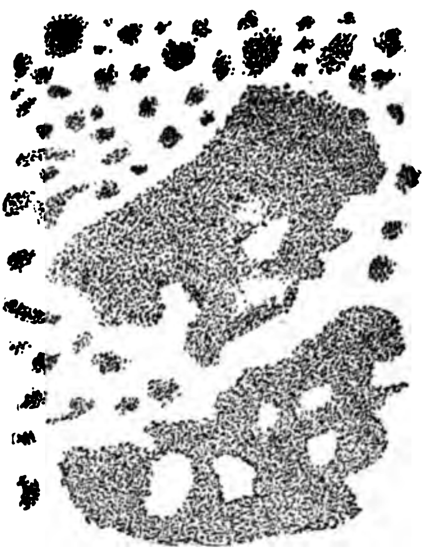

Fig. 24.—Sodium Urate, Amorphous (× 500).

the stomach and intestines, on the first day of menstruation, and in general malaise; and it may also occur in perfectly healthy individuals where the urine is highly concentrated. It is held in solution while the urine is warm, but quickly becomes precipitated upon cooling. It is the effete material of oxidation, the so-called *materia peccans* of old physicians.

In rare cases sodium urate is crystalline (see Fig. 25), appearing in the form of needle-like clusters or arranged like sheaves of wheat, or of a fan-shape arrangement, pointed toward the centre, and broader toward the periphery. This sediment has been found in various conditions, such as diseases of the stomach and intestines, and in healthy individuals during prolonged physical exertion. The accompanying illustration was taken from a case of dermoid cyst of the kidney, where the crystals occurred in large numbers with uric-acid crystals.

Sodium urate frequently undergoes a change a few hours after the urine is voided, the length of time required for the change depending upon

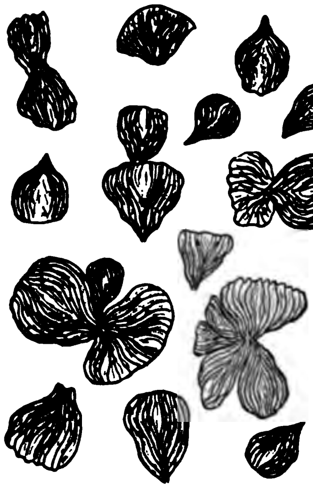

FIG. 25.—SODIUM URATE, CRYSTALLINE (× 500).

the temperature. The granules commence to change into small brown globules, which are either single or grouped in twos; the latter soon coalesce and form small dumb-bells, which gradually enlarge (see Fig. 26). This has been spoken of as the first stage of the formation of ammonium urate, *the ammonium urate in statu nascenti*, and denotes a commencing transition of the original acid sediment into an alkaline. When the alkaline change is more or less complete, we have the fully formed globules of ammonium urate.

3. CALCIUM OXALATE.—Calcium oxalate, when present in small or moderate amount in the urine, without an increase of specific gravity, has no clinical significance. Oxalic acid, normally present in all urine in small quantities, has a special affinity for calcium, and appears in the urine as calcium oxalate. It is frequently found after eating certain kinds of fruits and vegetables, such as apples, oranges, bananas, certain berries, grapes, tomatoes, rhubarb, asparagus, spinach, and turnips.

It occurs in a variety of forms (see Fig. 27), but it is always colorless and of a moderately high degree of refraction. The most common forms are those of quadrilateral octahedrons, greatly varying in size, with single or double lines running from one end of the crystal to the other, crossing each other in the centre and giving the characteristic so-called letter-envelope shape; when they are seen edgewise the octahedral form is more marked. These regular forms often commence to break down, so that the lines become lost. A number of the crystals may be arranged together, either in twos, giving the twin form, or in groups of three, four, or more. With these we often see small, more or less regular squares or dot-like irregular formations, the so-called amorphous shapes. A number of small squares may combine together, giving concretions sometimes of large size, which are especially abundant under the microscope when calcium-oxalate calculi are present. They are often massed together upon mucus-threads or foreign substances. Besides these, there are rarer forms, consisting of more or less concentrically striated, highly refractive discs or barrel shapes, and of variously sized dumb-bells. The latter may assume large proportions, and are easily differentiated from the dumb-bell forms of uric acid or ammonium urate, by their being colorless.

The common forms of calcium-oxalate crystals can hardly be mistaken for anything else, if it is borne in mind that they are always without color and of a moderate refraction. The small discs may be mistaken for red blood globules, but are of a considerably higher refraction than the latter. Although usually present in acid urine only, they may be found in am-

FIG. 26.—GRANULES OF SODIUM URATE CHANGING TO GLOBULES AND DUMB-BELLS (× 500).

photeric or faintly alkaline urine in small amount. When the reaction of an originally acid urine has become alkaline, they gradually disappear, while triple phosphates commence to develop. Should there be any doubt as to their character, they will be found to be insoluble in acetic acid, but soluble in hydrochloric acid.

When calcium oxalate is present in the urine in large amount, with a high specific gravity, 1.024, 1.030, or even 1.040, it often denotes the existence of *oxaluria*. This affection, although very common, is frequently overlooked. It gives the symptoms of neurasthenia, dyspepsia,

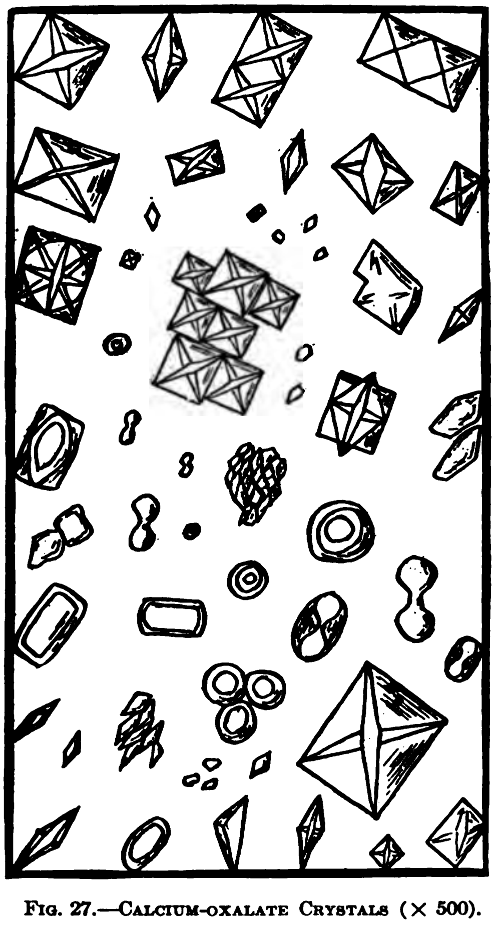

FIG. 27.—CALCIUM-OXALATE CRYSTALS (× 500).

melancholia, general malaise, headaches, and ill-defined pains in the lumbar region. Those afflicted are usually of sedentary habits and are accustomed to live well. In rare cases, especially when concretions of considerable size are present, hæmaturia, often severe and protracted, is a pronounced symptom. It may last for months, but its cause can at once be ascertained by an examination of the urine. As soon as the patient's diet is regulated and he takes considerable outdoor exercise, the oxalates decrease and the symptoms improve. With such cases inflammation of the pelvis of the kidney, and sometimes also of the kidney proper, though, as a rule, mild in character, is of common occurrence.

4. CYSTIN.—Cystin is a comparatively rare sediment, but may produce concretions in the bladder. It consists (see Fig. 28) of hexagonal, colorless plates of moderate sizes, of high refraction, which, in side view, present one perfect facet and two imperfect neighboring facets. A number of plates may lie together, one upon another, or they may form more or less regular masses. It is readily soluble in ammonia, one of the features distinguishing it from uric acid. Cystin contains considerable sulphur as a constituent.

Cystin seems to occur in all members of certain families instead of uric acid; in such families it appears to replace uric acid, and in them cystin calculi are not rare.

5. CREATININ.—Creatinin, normally present in the urine in very small amount, is found under the microscope in rare instances only. It consists

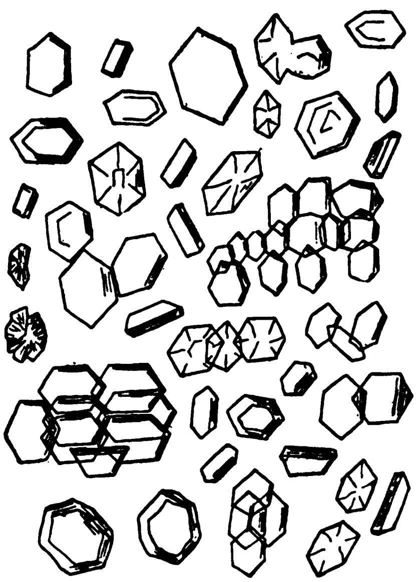

FIG. 28.—CYSTIN CRYSTALS (× 500).

(see Fig. 29) of colorless prisms or plates, partly lozenge- and partly barrel-shaped. Frequently there are two, three, or even more plates, one within the other, or the plates may conglomerate in groups. Occasionally, more particularly when the urine has stood for some time, peculiar configurations appear in the interior of the plates.

Creatinin is found most frequently after prolonged muscular exercise, as is seen in athletes during active training. A rare sediment, found in the urine of a perfectly healthy athlete, is shown in Fig. 30. This sediment contains plates and lozenges of creatinin, the rare crystalline form

FIG. 29.—CREATININ CRYSTALS (× 500).

FIG. 30.—SEDIMENT IN THE URINE OF AN ATHLETE (× 500).

of sodium urate, and peculiar formations, consisting partly of fan-shaped and partly of angular crystals, from which a varying number of long needles are seen to emanate. Some of these crystals resemble rarer forms of ammonium urate.

Clinically, creatinin has been found in cases of severe acute parenchymatous nephritis, associated with uræmic convulsions, and has also been seen in the urine in typhoid fever, pneumonia, and diabetes.

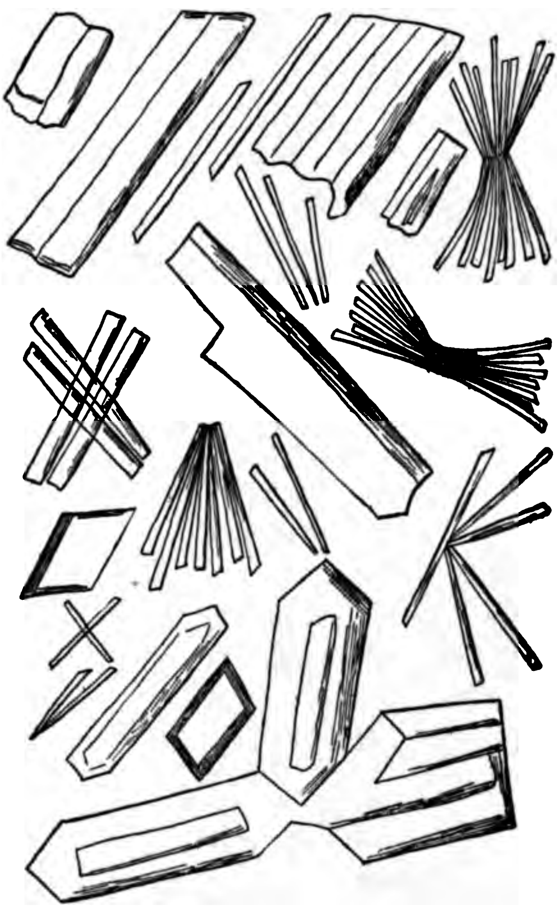

FIG. 31.—HIPPURIC ACID (× 500).

6. HIPPURIC ACID.—Hippuric acid, which is present in all normal urine, is almost always held in solution, though it may be found in small amount after a vegetable diet and after eating certain fruits, such as cranberries, plums, and prunes. In the urine of herbivorous animals,

especially in horses, it is of common occurrence. It is found in larger amount after the administration of benzoic acid or one of the benzoates, salicylic acid, cinnamic acid, and oil of bitter almonds. It has also been seen occasionally in diabetes.

It consists (see Fig. 31) of variously sized, colorless prisms and plates, often conglomerated into larger or smaller masses. The plates may be

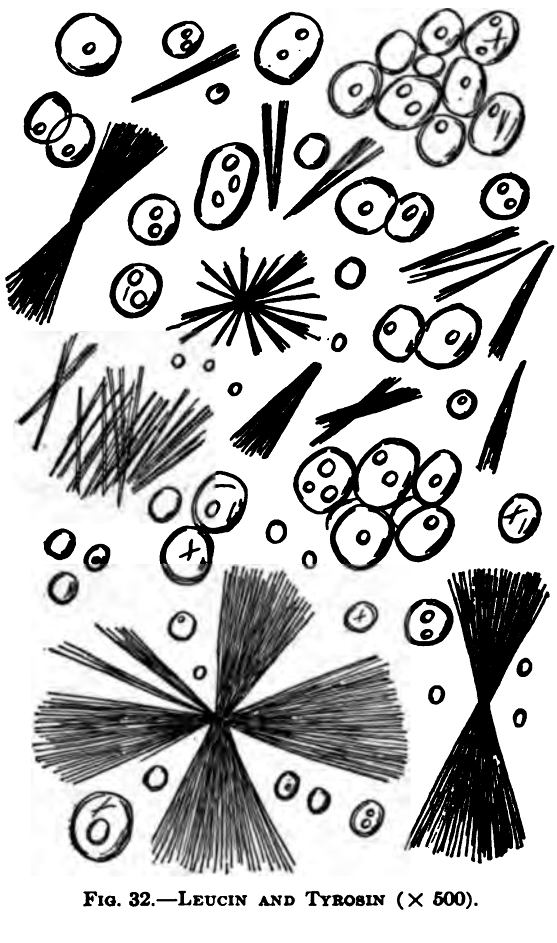

FIG. 32.—LEUCIN AND TYROSIN (× 500).

thin and extremely long, at times resembling needles. Hippuric acid might occasionally be mistaken for some forms of phosphates, but can easily be differentiated from them by its insolubility in acetic acid.

7, 8. LEUCIN AND TYROSIN.—Leucin and tyrosin are rare sediments, and usually occur together. They are never seen in normal urine, but mostly in severe acute and usually fatal diseases of the liver, such as acute yellow atrophy of the liver, phosphorus-poisoning, and in yellow fever. They have also been found in cases of smallpox, scarlet fever, and typhoid fever.

Leucin (see Fig. 32) appears under the microscope in the form of flat, yellowish or brown globules of different sizes, with delicate radiating and concentric striations. Tyrosin is found in the form of needle-shaped crystals, grouped in clusters or sheaves, crossing at various angles.

Both leucin and tyrosin somewhat resemble fat, the former the fat-globules, the latter the needles of fat—so-called margaric acid—but differ from fat by being insoluble in ether.

9. Calcium Sulphate.—Calcium sulphate (see Fig. 33) occurs in

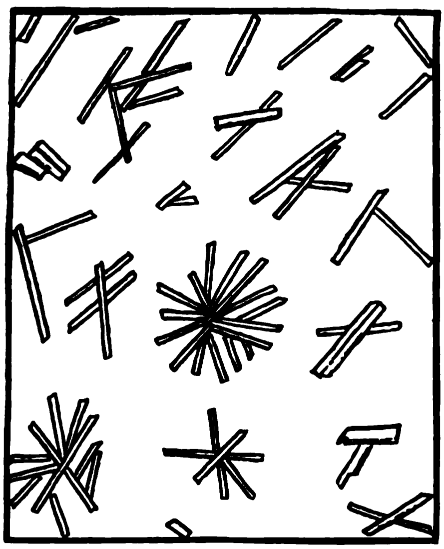

Fig. 33.—Calcium-sulphate Crystals (× 500).

urine in a small number of cases only, the specific gravity of the urine being, as a rule, high. It consists of thin, colorless prisms or needles, either single, in groups, or in rosettes, resembling crystalline calcium phosphate, but more regular. Its clinical significance is not known.

B. ALKALINE SEDIMENTS.

1. Triple Phosphates.—Triple phosphates, the combined ammonio-magnesian phosphates, may be divided into complete and incomplete. They may be found under the microscope in small numbers in urines which still give a faintly acid reaction, but invariably denote a change to

alkalinity. When present in large numbers, the urine is always alkaline. These phosphates are frequently secondary formations, not being seen when the urine is freshly voided, but being found in varying numbers a few hours later. They may be seen to develop while the urine is exam-

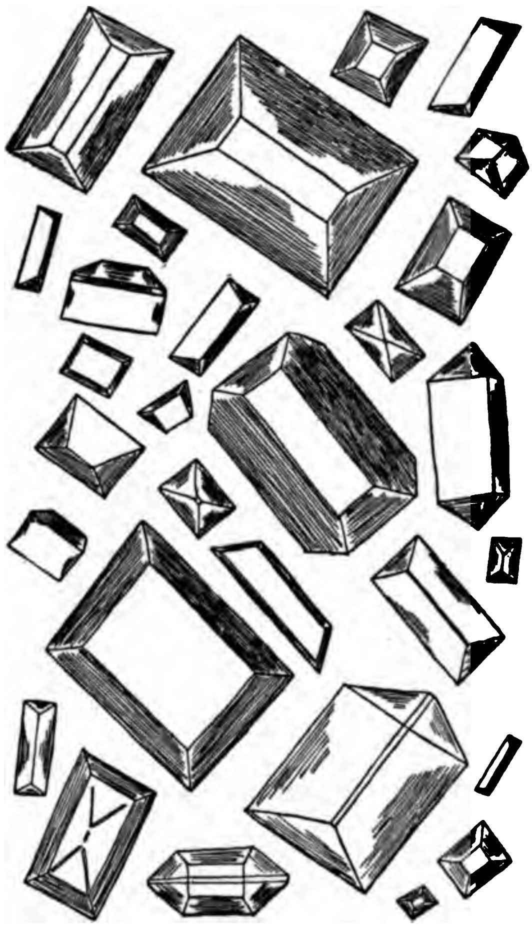

FIG. 34.—COMPLETE TRIPLE PHOSPHATES (× 500).

ined under the microscope. As all urates are colored to a greater or less degree, all phosphates are invariably colorless.

Complete triple phosphates (see Fig. 34) are colorless, triangular prisms or rhomboidal crystals, highly refractive, with bevelled ends—the so-called coffin-lid shapes. They vary greatly in size and shape, the latter being different when the crystals are seen in front, side, or top view.

Some of the smaller ones can hardly be differentiated from calcium oxalate crystals.

Incomplete triple phosphates (see Fig. 35) are seen in many forms and sizes. It seems that these crystals are in part not yet fully developed (especially the smaller varieties, which may in time grow and become

FIG. 35.—INCOMPLETE TRIPLE PHOSPHATES (× 500).

complete), and in part have become broken down from previously complete forms. All the different transitions can be seen in the same specimen when it is studied on two or three successive days, which can easily be done by simply adding a drop of glycerin to the urine upon the slide. The incomplete forms represent irregular plates, either without any distinct marks or with irregular lines, the result of the transformation of the complete crystals. The crystals may be broken down in the centre, or there may be peculiar cross-like formations, or even irregular star-shaped crystals, which can be likened to a fern leaf.

Triple phosphates may be found in varying numbers in normal urine after a vegetable diet. Their amount is increased in chronic inflammatory conditions of all kinds, in rheumatic processes, in inflammation of the bones, and in diseases of the nerve-centres. They are especially abundant in cases of chronic cystitis, where an alkaline putrefaction of the urine takes place in the bladder, and may be precipitated in large, flaky deposits, the urine having a pronounced ammoniacal odor.

2. Simple Phosphates.—Simple phosphates, or calcium phosphates,

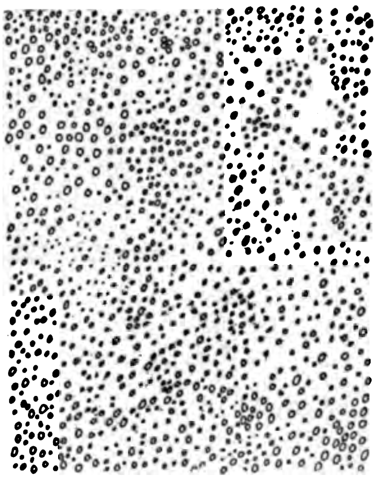

Fig. 36.—Amorphous Simple Phosphates (× 500).

are of two distinct varieties: first, amorphous; and second, star-shaped or stellate.

Amorphous simple phosphates (see Fig. 36) appear in the form of colorless globules or granules, of a moderate refraction, either single or clustered together in variously sized groups, but never in a moss-like arrangement, as the sodium urate. These phosphates are abundantly found after a milk diet, as well as after drinking different alkaline mineral waters.

Star-shaped or stellate simple phosphates, although of less frequent occurrence than the other variety, are by no means rare, and are often found in conjunction with the triple phosphates. They consist (see Fig. 37) either of slender, colorless rods or of pointed spicules of various sizes, at times larger and smaller ones being found together. Although they may be found single, their characteristic grouping is in the form of stars or rosettes, more or less complete. The spicules, of which the rosettes are composed, are united in the centre of the rosette, while each spicule

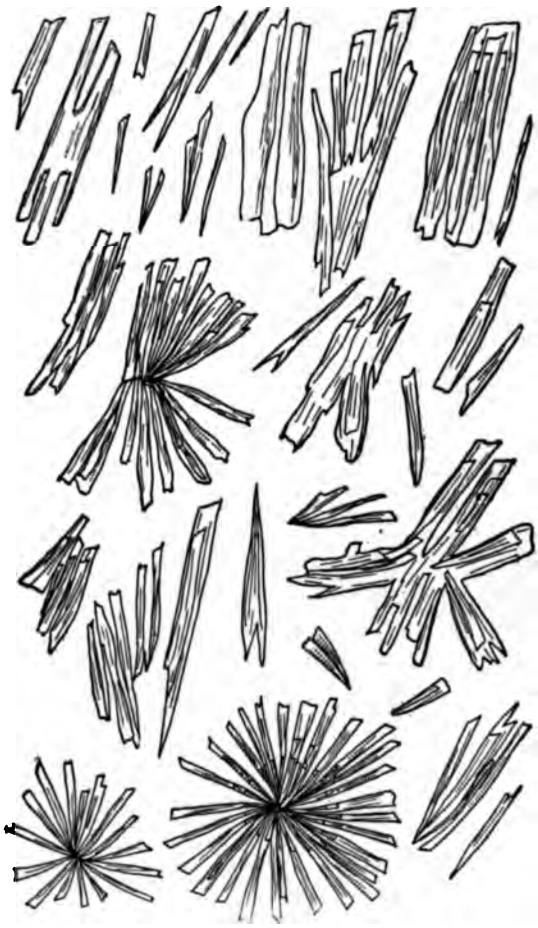

FIG. 37.—STAR-SHAPED SIMPLE PHOSPHATES (× 500).

may have a uniform diameter or be broadened at the periphery and narrowed in the centre.

Much has been written about the significance of the phosphates in the urine, and great stress has been laid upon their continual increase or diminution, the latter being said to be of constant occurrence in cases of nephritis. It is an undeniable fact that the phosphates are diminished in severe and usually advanced cases of nephritis, but not more so than the other salts, there being a pronounced decrease of all salts in such cases.

In rare cases there is a continual increase of the phosphates in the urine, without any apparent cause. Such cases have been designated by the term *phosphaturia*, and they may give similar symptoms to those of oxaluria. The phosphates precipitating in the urine being frequently

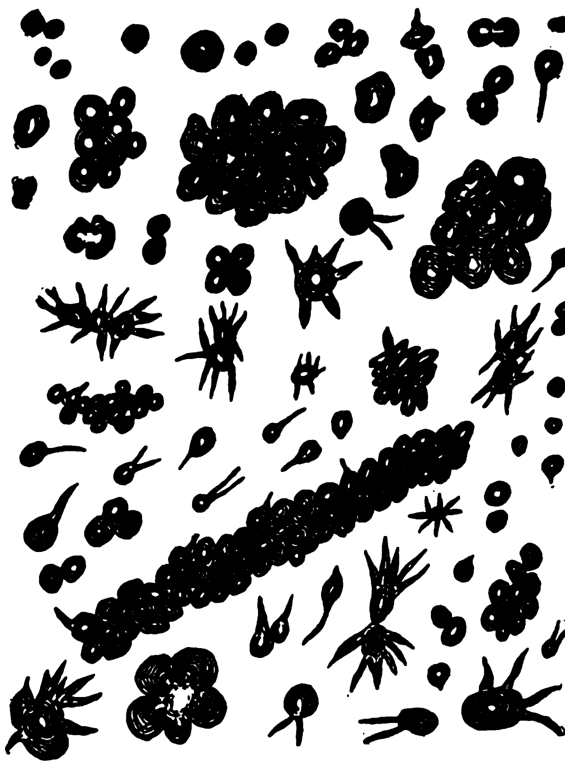

FIG. 38.—AMMONIUM URATE (× 500).

secondary formations, such a diagnosis must only be made when their amount is found to be greatly increased immediately after the urine is voided, and the presence of inflammatory conditions of any kind in the body can be excluded. A change of diet will often rectify this trouble in a short time. All phosphates are easily soluble in acetic acid, which will quickly clear up any doubts as to their character.

3. AMMONIUM URATE.—Ammonium urate is a common sediment in alkaline urine, especially in connection with triple and simple phosphates, and is seen in fresh urine only when it is passed in an alkaline condition.

It is the result of alkaline decomposition. It appears (see Fig. 38) in the form of brown globules of various shapes and sizes, usually exhibiting pronounced concentric and radiating striations. The globules may appear singly or in clusters, sometimes forming large, coalesced masses. They are either smooth or provided with thorny, sometimes branching

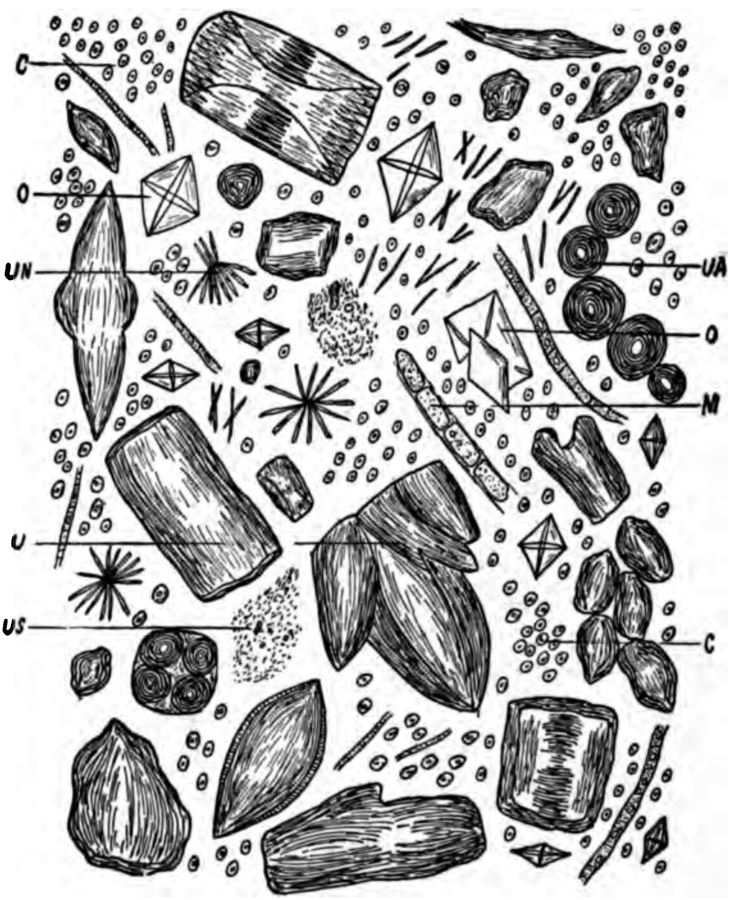

FIG. 39.—ACID SEDIMENT IN FERMENTATION AND IN TRANSITION TO ALKALINE (× 500). *U*, Uric-acid plates; *UN*, uric-acid needles; *US*, sodium urate in transition to globules and dumb-bells; *UA*, ammonium urate; *O*, calcium oxalate; *C*, conidia; *M*, mycelia.

and curved offshoots—the so-called thorn-apple shapes. The offshoots vary greatly in size and number, there being either one or many upon a single globule. Not infrequently the globules, especially the smaller ones, conglomerate so as to form concretions, sometimes of large size, and this may also be the case when mucus-threads or foreign substances, such as cotton or linen fibres, are present. Upon the addition of hydrochloric acid the globules of ammonium urate disappear and small rhombic crystals of uric acid are formed. Ammonium urate is soluble in alkalies, by the addition of which an odor of ammonia is evolved.

The alkaline change, which may take place in an originally acid urine, is illustrated in Fig. 39. When the urine was voided it contained nothing but a large number of uric-acid crystals of different forms, both plates and needles, some groups of sodium urate, and crystals of calcium oxalate. After about twelve hours fermentative changes commenced to appear, and fungi, in the form of conidia and mycelia, developed. The sodium-urate granules were now found to have partly changed into small globules and dumb-bells, possibly the first formed ammonium urate.

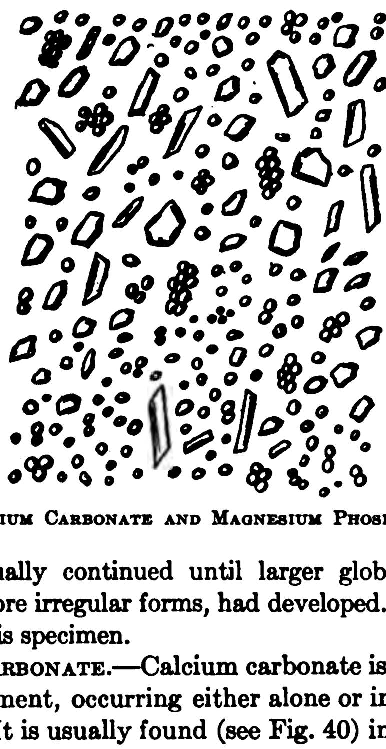

FIG. 40.—CALCIUM CARBONATE AND MAGNESIUM PHOSPHATE (× 500).

This change gradually continued until larger globules of ammonium urate, as well as more irregular forms, had developed. Triple phosphates were not seen in this specimen.

4. CALCIUM CARBONATE.—Calcium carbonate is a not very uncommon alkaline sediment, occurring either alone or in combination with the phosphates. It is usually found (see Fig. 40) in the form of amorphous granules and globules of different sizes, though mostly larger than the globules of amorphous simple phosphates; they are seen either singly or in groups of varying sizes, and are of very high refraction. Occasionally dumb-bell forms are also present, and very rarely small delicate prisms. By adding an acid, such as acetic acid, effervescence is produced, which also occurs in the presence of ammonium carbonate, though

this is always held in solution and never seen under the microscope. Calcium carbonate is the most common sediment in herbivorous animals, and the turbidity of their urine is due to its presence.

This salt appears mainly in inflammatory and carious processes of the bony system, such as osteitis, osteomyelitis, osteomalacia, and rhachitis. It may also be found in diabetes and phthisis. After drinking certain mineral waters in large quantities it may be seen in the urine.

5. MAGNESIUM PHOSPHATE.—Magnesium phosphate (Fig. 40) is an extremely rare sediment, producing colorless, highly refractive, elongated, quadrilateral prisms, sometimes resembling the small plates of incomplete triple phosphates. It is observed in the urine after the internal use of the fixed alkali-carbonates, such as are held in solution in many mineral waters, and may be found with calcium carbonate. It is readily soluble in acetic acid.

II. *OTHER UNORGANIZED SEDIMENTS.*

Fat.—Fat, in the form of globules and granules, is of common occurrence in the urine, but care must be taken not to confound it with

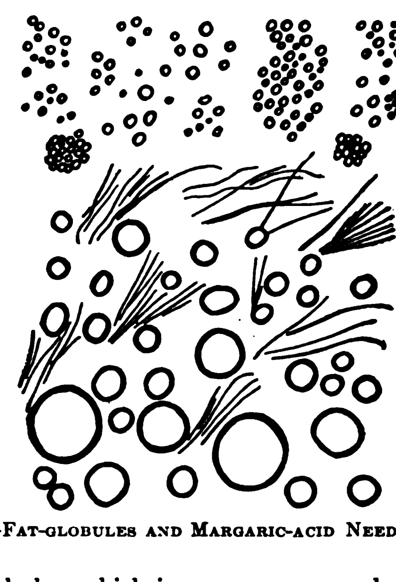

FIG. 41.—FAT-GLOBULES AND MARGARIC-ACID NEEDLES (× 500).

extraneous fat-globules, which in many cases are larger, more irregular, and of a more yellowish color. If fat is not present in too large quantities, the microscopical appearance of the urine is not changed, but if it exists in large amount, as, for instance, in the rare cases of *chyluria*, in connection with considerable albumin, the urine is turbid or milky when voided, and, after standing, a peculiar creamy layer appears at the top of the urine. When fat-globules are voided in such large quantities as to be seen with the naked eye, and albumin is either entirely absent or present in small amount only, the diagnosis *lipuria* is justified; these cases are, however, just as rare as those of chyluria. The addition of a few drops of ether clears up the urine to a certain degree.

Fat-globules and -granules vary considerably in size (see Fig. 41). When the larger globules are found, needles of margaric acid may also be present; these are long, slender formations, in which a double contour can be seen only in rare instances. They lie between the globules, as well as within them in some cases, and may also appear to emanate directly from them. Fat-globules have a high refraction and usually a rather dark contour.

Leaving out of consideration the rare cases of chyluria and pronounced lipuria, the latter of which has been observed in healthy individuals temporarily after a highly fatty diet, as well as in pregnant women and in cases of phosphorus-poisoning, the appearance of a small or moderate number of small fat-globules and -granules, either singly or in variously sized groups, is seen in all cases in which a chronic inflammation, even of mild character, exists somewhere in the genito-urinary tract. These globules are not only found lying free throughout the different fields, but in varying numbers within the epithelia and pus-corpuscles, being undoubtedly secondary products of the protoplasm. The globules may make their appearance in small numbers a few weeks after the commencement of the inflammation, but are found in greater quantity only in chronic cases; the more numerous the globules, the more pronounced the inflammation. At first, one or two glistening globules of very small size are seen in the granular protoplasm, which condition becomes more and more pronounced, until the fatty degeneration, in severe cases, attacks the whole of the epithelium, occasionally changing its appearance completely.

Such fat-globules are, therefore, found not only in chronic cases of nephritis and pyelitis, but also in cystitis, prostatitis, urethritis, and vaginitis. In the different varieties of nephritis their numbers vary greatly. When present in small or moderate numbers only, no other diagnosis than that of a chronic inflammation is justifiable; but if very abundant, either with or without the presence of fatty casts, a diagnosis of fatty degeneration can be made.

Cholesterin.—Cholesterin, a normal ingredient of bile, is occasionally found in the urine. It consists (see Fig. 42) of colorless, thin, irregular rhomboidal plates, frequently broken in different parts and of greatly varying sizes. It easily dissolves in ether, and takes on a reddish or violet color if treated with iodine and a drop of a sulphuric-acid solution.

Cholesterin has been found in a few cases of chronic cystitis, in rare cases of chronic parenchymatous nephritis with fatty degeneration, and in chyluria. Its exact significance is unknown.

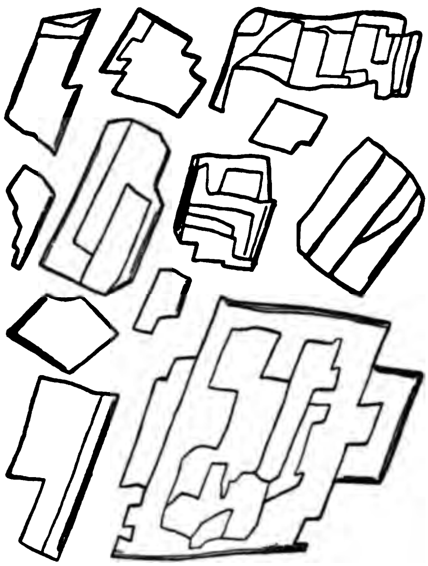

FIG. 42.—CHOLESTERIN CRYSTALS (× 400).

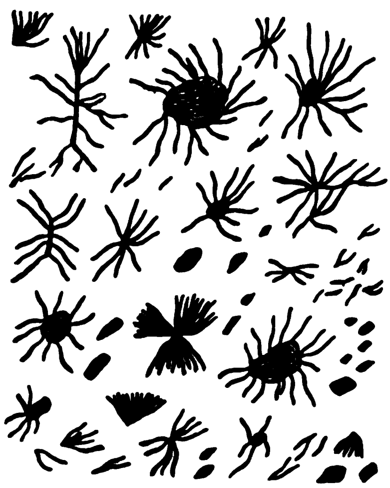

FIG. 43.—HÆMATOIDIN CRYSTALS (× 500).

Hæmatoidin.—Hæmatoidin crystals seem to be the result of extravasated blood, if retained within the tissues. They appear in the urine (see Fig. 43) in the form of small, irregular plates, as well as needle-shaped, sometimes stellate, crystals of a reddish-brown or, rather, rust-brown color. The needle-shaped crystals vary considerably in size, and may be found either singly or in conglomerations of peculiar forms. Not only may the needles be arranged so as to form bunches resembling the bristles of a brush, but an irregular mass may be surrounded by a large number of needles, sometimes giving a crab-like appearance. The larger formations are rare, while the smaller are comparatively common, not only lying free, but also in the interior of pus corpuscles and epithelia. Their presence always denotes a hemorrhage which has taken place at some previous time, and they may, therefore, be found in a variety of different lesions.

Besides hæmatoidin, it is claimed that *bilirubin* may be found under the microscope, closely resembling the crystals of hæmatoidin, and seen in both plate and needle form. They are usually larger and more irregular than the former, and their relationship is still undecided.

Indigo.—All normal urine contains a small amount of indican, and the indigo occasionally found in the urine is, as a rule, a secondary prod-

FIG. 44.—INDIGO CRYSTALS (× 500).

uct of oxidation, often seen when putrefactive changes have developed. In rare cases the urine has a bluish color when voided, the indigo having been formed in the body; this is seen in pathological conditions only.

Indigo (see Fig. 44) is seen in the form of blue rhomboidal crystals of small size, or irregular masses, as well as in needles and thin plates. Although it was formerly always considered to have a pathological significance, it is now known to be present in perfectly normal conditions. It is not uncommon to see indigo under the microscope in small amount as extraneous matter from the underwear, and this cannot, in most cases, be distinguished from that formed in the urine.

Melanin.—Another coloring matter which at times is seen in the urine is melanin, appearing as dark brown or perfectly black, irregular granules or masses of small size. It has been found in melanotic tumors, such as sarcoma and cancer, as well as in broken-down constitutions due to various troubles, and cannot be said to have any special significance.

After intra-vesical injections of silver salts, such as argyrol, the urine may contain black granules and masses of varying sizes, which microscopically cannot be differentiated from melanin. These granules may be found in smaller or larger numbers, both in free groups, irregularly scattered, and upon pus corpuscles and epithelia.

URINARY CONCRETIONS.

Quite frequently concretions may form in the urinary passages and be found in the urine. When very small, these concretions are called gravel; when large, stones or calculi. The former can be passed in large amount with little or no pain; the latter cause great suffering and the condition may require surgical interference. Concretions are formed either in the kidney, pelvis of kidney, or bladder, and most frequently consist of uric acid, urates, calcium oxalate, or phosphates. Besides these, concretions of cystin and calcium carbonate, as well as indigo and xanthin, may be found.

Concretions may consist of one ingredient only, or of two or more in alternate layers. The majority of concretions have a central portion or nucleus and a peripheral portion or body. The nucleus varies in size and composition. It may consist of the same material as the body, though, as a rule, some organic product, such as a blood clot or mucus-thread, will form the nucleus, around which the body of the calculus forms. In rare cases, foreign bodies introduced into the bladder from outside become the nuclei of stones.

The most common are the uric-acid concretions, which may be passed in large amount in the form of gravel, but often attain a large size. They compose from seventy to eighty per cent of all concretions, and are formed either of uric acid alone or combined with the urates; are hard, and have a yellowish-brown or reddish-brown color. Calcium-oxalate concretions have a grayish or dark color, and may be either small, round, and smooth—called hemp-seed calculi—or large, rough masses—the mulberry calculi. Sometimes the nucleus of these concretions consists of uric acid. Phosphatic concretions are usually formed of mixed triple phosphates and calcium phosphates. They are mostly of large size and have a grayish-white color. Other concretions are of rare occurrence.

In many cases their nature can easily be determined by placing a minute particle in a drop of glycerin under the microscope.

Although the presence of concretions, even when very minute, can almost invariably be determined by microscopical examination of the urine, a number of examinations must not infrequently be made before the diagnosis becomes positive. The first urine examined may contain a small number of salts only, or these may be entirely absent under the microscope, though subsequent examinations will show them in large amount and clear up any doubt. In all such cases inflammations or hemorrhages from the kidney, pelvis of kidney, or bladder will sooner or later develop.

For a more detailed analysis, the concretions should be powdered and subjected to a red heat upon platinum foil. If the odor of hydrocyanic acid is given off, the concretion contains either uric acid or xanthin, the latter of very rare occurrence. Uric acid gives the characteristic murexide test; xanthin does not. If considerable residue of ash is left, which when heated to a high temperature melts to a white mass, it contains phosphates; phosphatic concretions are soluble in hydrochloric acid without effervescence. If the powder first blackens upon heating, but upon further heating leaves considerable white ash, which dissolves in hydrochloric acid with effervescence, it contains calcium oxalate; if this solution is neutralized with ammonia, and oxalic acid is added, characteristic envelope-shaped crystals, which are readily recognized under the microscope, are precipitated. If the powder upon burning emits an odor of sulphurous acid and burns with a bluish flame, it contains cystin; when ammonia is added to the powder it dissolves, and upon evaporation crystallizes in hexagonal plates easily diagnosed by the microscope. Calcium-carbonate concretions dissolve in hydrochloric acid with effervescence. In order to ascertain if a calculus consists of more than one ingredient, it is best to section it and examine the powder from each layer separately.

CHAPTER X.

BLOOD-CORPUSCLES AND PUS-CORPUSCLES.

I. *BLOOD-CORPUSCLES.*

Red blood-corpuscles or *red blood-cells* are of common occurrence in the urine; they may be derived from any portion of the genito-urinary tract. When present in small numbers, the urine is either not changed in color or it is cloudy, turbid or smoky; but when they occur in large numbers, the urine has a reddish hue and may be of a dark red or deep brown color, the condition being then known as *hæmaturia.* During the period of menstruation red blood corpuscles occur normally in the urine of females, but with this exception their appearance invariably indicates some abnormal condition.

Red blood-corpuscles, as found in the urine, vary considerably in appearance, shape, and size (see Fig. 45). In fresh urine they are discoid bodies of a yellowish hue and frequently crenated, but after a few hours only may have entirely lost their hæmoglobin and are then practically colorless. This change takes place more quickly in alkaline than in acid urine, and also depends upon the degree of concentration of the urine. As long as the blood-corpuscles contain considerable hæmoglobin, they have a yellowish color; as soon as they commence to lose their coloring matter, a double contour can usually be seen, the interior being in most cases apparently structureless. This is the condition in which they are most frequently found.

When they are present in large numbers, they are found both singly and conglomerated in variously sized masses, and the so-called thorn-apple shapes are often seen. When they lie edgewise they appear biscuit-shaped, and may be found in small masses like rolls of coin; the latter is comparatively rare in urine. As a rule they are neither granular nor nucleated, and can thus easily be distinguished from pus-corpuscles, even if the double contour is not well marked. In acid urine, however, after it has been standing a few days, a small number may appear granular and quite irregular.

Unless blood-corpuscles are present in very small numbers only, every urine containing them will also contain an appreciable amount of albumin. In severe cases of hæmaturia the amount of albumin may reach one-half of one per cent or more, and still the kidneys be perfectly normal, the blood coming perhaps from the bladder, the urethra, the prostate gland or the seminal vesicles.

When the urine is of a low specific gravity, the red blood-corpuscles frequently swell and become hydropic. In such cases they are large, pale, double-contoured bodies, and are called "ghosts." In an active hemorrhage, besides the corpuscles described, small globules are frequently

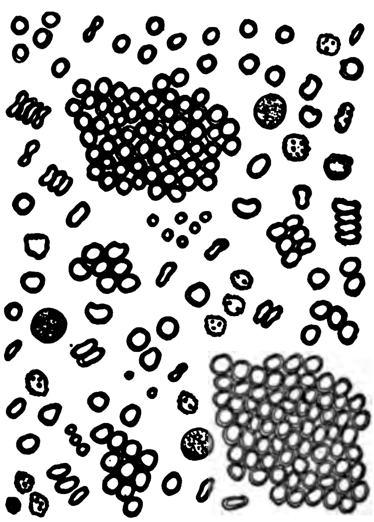

FIG. 45.—BLOOD-CORPUSCLES (× 500).

seen, which are sometimes less than half the size of the regular corpuscles, but perfectly characteristic. These are of recent formation, are immature red blood cells, and may be called hæmatoblasts.

Whenever a large number of red blood-corpuscles is present in the urine, a small number of *white blood-corpuscles* or *leucocytes* is invariably seen. They vary in amount, but average one of the latter to five hundred or six hundred of the former. Leucocytes cannot be distinguished from pus-corpuscles. They are usually found in the form of globular, granular bodies, which may or may not show a nucleus, though they can easily change their form on account of the contractility of their protoplasm. When a hemorrhage exists and these corpuscles are seen in small numbers only, they should not be mistaken for pus-corpuscles.

In an active hemorrhage we frequently notice, besides blood-corpuscles, *fibrin*, as well as *clots of blood* (see Fig. 46).

Fibrin appears either in the form of thin, pale, colorless strings, or larger, more or less reddish or brown masses, frequently giving off smaller branches. It always consists of wavy bands, of a higher refraction at the periphery than in the centre, and of a characteristic appearance. When large, the masses can easily be seen with the naked eye. In rare cases, such as severe hemorrhages due to tumors or parasites, they may attain enormous sizes. Not infrequently they resemble cast-like structures or even form distinct casts.

Blood-clots consist of irregular, rust-brown or dark masses, varying in size, which are composed of disintegrated blood-corpuscles; they may be so dense that their structure cannot be made out, and they must be diagnosed from their color.

When blood-corpuscles, even in small numbers, are present in the urine, it is absolutely essential to discover their source. This can only be determined by the nature of the epithelia in the urine. As long as the hemorrhage is mild or of moderate severity only, epithelia can al-

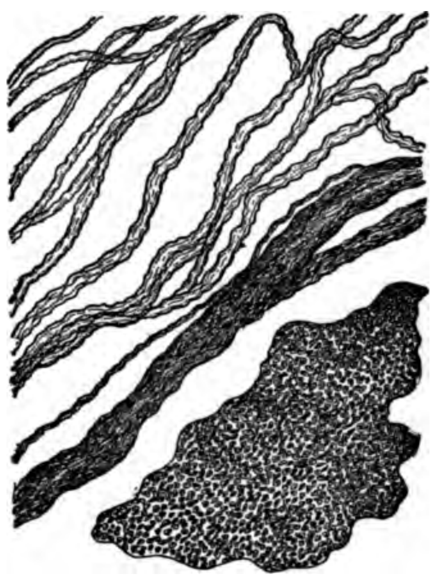

FIG. 46.—FIBRIN AND BLOOD-CLOT (× 500).

ways be found without any difficulty; but in the worst cases of hæmaturia, where many fields of the microscope may be crowded with blood-corpuscles, it is at times quite difficult to find epithelia. In these cases many drops of urine must sometimes be examined before the source of the hemorrhage can be positively determined. Some authors advise the removal of the blood from the sediment by the addition of a large amount of lukewarm water and a few drops of dilute acetic acid, stirring thoroughly and allowing to settle. This process undoubtedly changes many of the other elements present in the sediment, and it is best not to use it unless absolutely necessary. A much better plan is to dilute a drop of urine upon a slide with a drop of chemically pure glycerin; this causes some of the masses of the red blood corpuscles to become separated and paler, so that the search for epithelia is liable to be more successful.

The color, reaction, and specific gravity of the urine can never afford any positive clew as to the source of the blood, and the nature of the hæmaturia will only occasionally help in clearing up the case. In hæmaturia of urethral origin, due either to inflammations or traumatic conditions, the blood oozes from the urethra between the acts of micturition or may be squeezed out. In such cases, as well as in inflammations of the prostate gland or seminal vesicles, the first portion of urine voided is liable to contain more blood than the last, which may even be practically free from blood. In hemorrhage from the bladder, the blood is apt to be more abundant toward the end of micturition, while in hemorrhage from the upper urinary tract the blood is liable to be evenly distributed, so that when the urine is voided into two glasses, both will contain an equal amount of blood. Again, irregular blood clots, sometimes of large dimensions, are more frequently present in vesical hæmaturia, though occasionally fair-sized clots may be seen in hemorrhage from the upper urinary tract.

The pathological conditions in which blood-corpuscles are found are numerous. They are present in small or moderate numbers in every acute inflammation, whether of mild or severe character, and even in simple irritations and congestion. They will be found in a prostatitis as well as in a nephritis; also in pyelitis, ureteritis, cystitis, urethritis and spermato-cystitis. The presence in the urine of an abnormally large amount of salts may be sufficient to set up an irritation of the kidney or pelvis of the kidney with the appearance of blood-corpuscles.

Hemorrhages from the genito-urinary organs are of comparatively frequent occurrence and due to many causes. Perhaps among the most common of these cases are hemorrhages from the pelvis of the kidney, often due to gravel or calculi. Severe inflammations, abscesses, ulcers, tumors, stricture of the urethra, or traumata of different kinds, as well as parasites, will cause them. In tuberculosis of any part of the urinary tract, as well as of the prostate gland and seminal vesicles, hæmaturia is a common symptom; in this condition the attacks of hemorrhage are frequently intermittent, although they may continue over a long period. A little care exercised in discovering all the features present in the urine will in most cases lead to a positive diagnosis of the source of the hæmaturia.

Hemorrhage from the kidney itself occurs frequently enough and may be due to numerous causes. It may be found in simple renal congestion, as well as in acute and chronic nephritis, in abscess, tuberculosis, concretions or calculi, neoplasms, especially malignant tumors, different degenerations, also in embolism of the renal artery and thrombosis of the renal vein. Renal hæmaturia may be present in the malignant forms of the acute infectious diseases, such as scarlatina, variola, yellow fever, typhus and relapsing fevers, Asiatic cholera, in typhoid fever, malaria and other conditions; also in blood diseases, such as pernicious anemia and the leukæmias, furthermore in purpura hæmophilia and scurvy. It may be quite pronounced in cases of acute nephritis due to poisoning with different drugs such as carbolic acid, cantharides and turpentine, and has been observed during the administration of urotropin and other drugs. The presence of parasites, such as the filaria sanguinis hominis, distoma hæmatobium and echinococcus may cause it, and it may also be due to traumatism.

An *idiopathic form* of renal hæmaturia has been described, also called *essential hæmaturia*, in which the hemorrhage occurs without apparent cause. Some of these cases are probably angioneurotic; not infrequently a dilatation of the renal blood-vessels, that is a teleangiectasis is here present, and sometimes a true angioma. The term *renal hæmophilia* has also been applied to these cases, and the hæmorrhage is usually intermittent.

II. *PUS-CORPUSCLES.*

Whenever *pus-corpuscles* are present in the urine, even in small numbers, an abnormal condition exists somewhere in the genito-urinary tract. If they are very scanty, this condition is not necessarily an inflammation, though there is undoubtedly an irritation in some portion of the tract. As soon as they are found in at least moderate numbers, the diagnosis of an inflammation can at once be made, which is the more pronounced the greater the number of pus-corpuscles; when they are very numerous we may even be justified in diagnosing suppuration, though not without other features.

Urine containing pus-corpuscles in small numbers may appear perfectly normal to the naked eye, but the greater their number the more turbid it becomes, and in urine in which they are abundant a heavy, grayish-white sediment will sink to the bottom in the course of a few hours. In such cases the term *pyuria* might be properly used. Every urine in which pus-corpuscles are present in any appreciable number contains albumin, no matter from what organ they are derived, and the larger the number of pus-corpuscles the greater the amount of albumin.

The term "pus-corpuscles" is really a misleading one, since the presence of these cells does not necessarily signify the presence of true pus; they are found in the urine in every inflammatory condition, even in the mildest, though in mild cases they are seen in small numbers only. The greatest numbers of so-called pus-corpuscles are emigrated white blood-corpuscles, hence the two terms of "pus-corpuscles" and "leucocytes" are frequently used synonymously. All of these corpuscles, however, are by no means derived from the blood-vessels through emigration; some are derived from lymph-vessels or lymph-channels, still others from the connective-tissue cells through prolifera-

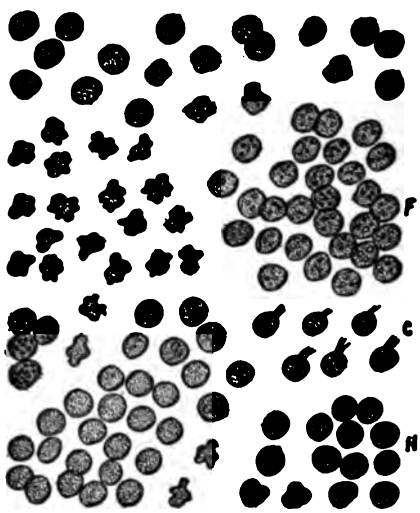

FIG. 47.—PUS-CORPUSCLES (× 500).
F, Pus-corpuscles with fat-globules; *C*, ciliated pus-corpuscles; *H*, pus-corpuscles with hæmatoidin crystals.

tions and new-formation, and some may even be derived from the epithelia through proliferative changes of their nuclei. The so-called pus-corpuscle therefore is a cell due either to emigration or to proliferation as the result of some irritation and stimulation. As long as such a corpuscle remains in connection with the tissues, it is known as an inflammatory corpuscle, but as soon as it leaves the tissues and is present in an excretion, such as the urine, it is called a pus-corpuscle. When these cells are present in large numbers in the tissues, and, when with an excessive emigration of leucocytes there is also a destruction of tissue elements, true pus is formed. In such cases pus-corpuscles are very abundant in the urine, and the term *pyuria* is justified.

The presence of so-called pus-corpuscles in urine therefore simply signifies the presence of some abnormal condition somewhere in the genito-urinary tract, which may be a mere irritation or mild inflammation, a severer inflammation, a suppurative or even an ulcerative process, in accordance with the numbers of these cells as well as in accordance with other features giving evidences of the character of the pathological lesion.

Pus-corpuscles in urine appear mostly as small, round, granular bodies, perhaps twice the size of normal red blood-corpuscles, in which one or more nuclei may or may not be seen. In freshly voided urine pus cells not infrequently exhibit active amœboid changes, assuming a variety of irregular forms (see Fig. 47).

In dilute as well as in highly alkaline urine the pus-corpuscles swell and assume a large, globular shape, becoming hydropic. In these a central nucleus will be observed, while the granulations around the peripheral portions become pale or almost entirely disappear. In some cases the nucleus breaks up into a number of small globules,

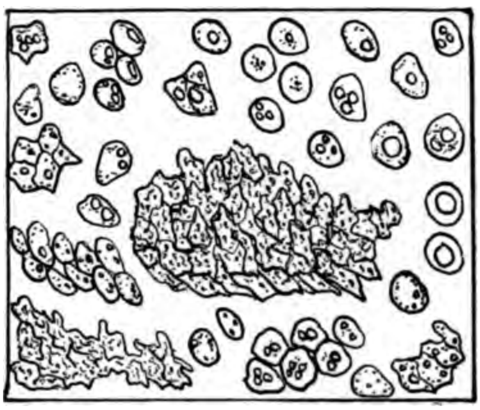

FIG. 48.—PUS-CORPUSCLES SHOWING VARIOUS CHANGES (× 500).
Individual corpuscles enlarged, swollen, hydropic, nuclei degenerated; masses found in ammoniacal decomposition.

which may remain in the centre of the cell or be pushed toward its periphery. The granules may disappear completely so that the entire cell appears like a structureless body, or the granules are still seen along the periphery of the cell. In ammoniacal urines, as seen in chronic cystitis, the pus-corpuscles, when present in large numbers, burst and coalesce, producing a sticky mass, which can be transferred to the slide only in jelly-like lumps (see Fig. 48). In such cases a large amount of mucus is always present, and it may become almost impossible to differentiate the pus-corpuscles from mucus-corpuscles.

The apparent presence or absence of nuclei in the pus-corpuscles depends entirely upon the amount of granulation; in coarsely granular corpuscles they are invisible, but become well marked when the granulation is fine. Not infrequently varying numbers of small, glistening fat-globules and granules appear in the pus-corpuscles, and this fatty change may be so pronounced that almost the entire granulation is altered. Such a pronounced change always denotes a chronicity of the inflammation, although the fat-globules may commence to appear a few weeks after the beginning of the inflammation, when the process cannot as yet be called strictly chronic. In perfectly acute inflammations, however, they are never found, except in some intoxications, such as poisoning with phosphorus.

Sometimes pus-corpuscles are seen which contain delicate, rust-brown crystals of hæmatoidin, in both needle and plate form. This is more especially the case in those derived from epithelia of the pelves of the kidneys and the uriniferous tubules of the kidneys, and denotes a previous hemorrhage. In recent hemorrhages the pus-corpuscles may have a uniform yellow color, due to the imbibition of the coloring matter of the blood. A similar diffuse yellow color of the pus-corpuscles is seen when bile is present in the urine, and in pronounced cases of choluria the color of the pus-corpuscles may be yellowish-brown or greenish-yellow. In cases of chronic catarrhal cystitis, dark brown pigment granules may sometimes be found in the pus-corpuscles. Occasionally pus-corpuscles which have delicate hairlike prolongations—cilia—are seen. These arise from the ciliated columnar epithelia of the uterus, and when present justify the diagnosis of an endometritis. Care must be taken not to mistake bacteria adhering to the surface of the pus-corpuscles for cilia.

Pus-corpuscles may be derived from any portion of the genito-urinary tract, and their source can only be determined by the nature of the epithelia present in the urine. Being invariably found in every inflammation, the mildest as well as the most pronounced, they are among the most common of all the elements found in the urine. To diagnose an inflammation of the kidney, it is by no means necessary to find casts, since a number of kidney lesions, sometimes quite severe in character, exist without the presence of casts. Irritation from a large number of salts, which is common in the pelvis of the kidney, is sufficient to show a small number of pus-corpuscles. Although highly alkaline urine frequently accompanies an inflammation of the bladder, no positive conclusion can be arrived at without the characteristic epithelia. Again, in the urine of a female a large number of pus-corpuscles may be present without any other trouble than a vaginitis, though this may be sufficient for an appreciable amount of albumin to appear. The same may be said of prostatitis and urethritis. Any doubt as to the origin of the pus-corpuscles will at once be dispelled by finding the characteristic epithelia in the urine.

From what has been said no difficulty should be encountered in diagnosing pus-corpuscles when they are present, even in small numbers, though it must be remembered that they are bound to vary in size and appearance in different cases, and to a small degree even in the same case. Their differentiation from the smallest epithelia, especially the kidney epithelia, when the latter are present in small numbers only, may not always be easy. Kidney epithelia, however, are distinctly larger than the largest pus-corpuscles in the same case, provided that these corpuscles have not become hydropic. When they are hydropic they may become quite large, but then are always pale and finely granular or have lost their granules more or less completely. Kidney epithelia, on the other hand, are distinctly granulated, and, as a rule, have a fairly large, distinct, usually centrally located nucleus.

When an ammoniacal decomposition has set in, which often enough occurs in cases of chronic cystitis, the pus-corpuscles may have become more or less completely changed, and converted into a gelatinous or jelly-like mass, in which characteristic corpuscles cannot be recognized any more. In such cases it may be of advantage to apply certain tests for a positive recognition of their presence. A simple test is that of *Vitali:* Acidify the urine with acetic acid and filter; treat the contents of the filter with a few drops of tincture of guaiac, when a deep blue color appears in the presence of pus. If it is impossible to filter the urine on account of its thick, ropy character, place a small amount of the urine in a test tube, and allow a few drops of tincture of guaiac to flow upon the surface. If pus is present a distinct blue line of contact will be observed.

The knowledge of the fact that in ammoniacal urine pus becomes transformed into a gelatinous mass, due to the action of ammonium carbonate, has been utilized by *Donné*, whose test for the presence of pus in a suspected urine consists in treating the urine or its sediment with a few drops of a concentrated solution of sodium or potassium hydrate, when, in the presence of pus in small amounts the liquid becomes mucilaginous and ropy, in larger amounts converted into a gelatinous, mucus-like mass, which adheres to the bottom and sides of the test tube.

The so-called iodine-reaction of pus corpuscles sometimes gives positive results but as a rule only in intense pathological conditions.

A drop of the urine-sediment upon a slide is mixed with a drop of an iodine-iodide of potash solution such as Lugol's solution. Owing to the presence of glycogen, the pus-corpuscles after such treatment may stain a dark mahogany brown, while the epithelia, which may resemble them, assume a light yellow color. This test when positive is quite characteristic, but often enough, especially in simple inflammations, it cannot be obtained.

CHAPTER XI.

EPITHELIA.

WITH very few exceptions, epithelia present in the urine always denote a pathological process of some kind. Normally the only epithelia found in urine are irregular, flat epithelia from the bladder, in small numbers, while in urine of females there may be flat epithelia from the vagina; the presence of all other epithelia is pathological. Although it is claimed to be impossible to diagnose the sources of the different epithelia in the urine, this is not at all difficult, provided a few general points are always borne in mind; and it is only by an accurate knowledge of their sources that we are able to obtain a diagnosis of the location of the morbid process. Most of the morbid processes occurring along the genito-urinary tract are inflammatory in nature, and marked by the presence of pus-corpuscles in the urine, and the location of the inflammation is determined by the epithelia.

Before speaking of the nature of the different epithelia found in the urine, it is necessary to have an idea of the general characters of the epithelia occurring in the body. These are of three kinds: First, *flat* or *squamous;* second, *cuboidal;* and third, *columnar* or *cylindrical.* Flat epithelia are always more or less irregular in outline, exhibiting a broad front surface, while in edge view they are narrower and somewhat spindle-shaped. Cuboidal epithelia have about the same diameter in all directions, while columnar epithelia are elongated in one direction. The latter may be ciliated, having one or more delicate, hair-like prolongations on the outer surface. All epithelia are granular and possess one or more nuclei, which, however, need not always be visible and may have dropped out, leaving a vacuole. The granulation may be coarse or fine, the flat epithelia being frequently more finely granular and paler than the others.

All epithelia may occur either in a single layer or stratified; that is, there may be a number of different layers. Wherever stratified epithelia occur and all three varieties are present, the flat variety is seen to compose the outer or upper layers, the cuboidal the middle layers, and the columnar the inner or deepest layer, nearest to the connective tissue.

In the genito-urinary tract a lining of stratified epithelium is found in the pelves of the kidneys, the ureters, bladder, urethra, vagina, and cervical portion of the uterus, while a simple epithelial lining exists in the uriniferous tubules of the kidneys, the prostate gland, seminal vesicles, ejaculatory ducts, Bartholinian gland, and mucosa of the uterus.

It is maintained that the epithelia from different organs, such as the bladder, ureters, and pelves of the kidneys, are identical in size and shape. By scraping off the epithelia of these organs, this idea appears correct; but if the epithelia are examined *in situ*, we will soon be convinced that their sizes vary considerably. The largest epithelia are found in the vagina; the next in size in the bladder; then, in order, those of the cervix uteri, urethra, pelves of the kidneys, ureters, and prostate gland; the smallest in the uriniferous tubules. It must not be forgotten, however, that there are transitional sizes, which are of no value for diagnosis. The smallest cuboidal epithelia from the bladder, for instance, may be identical with the largest cuboidal epithelia from the pelves of the kidneys, but the average size is absolutely different, being considerably smaller in the pelves than in the bladder. Again, the caudate and lenticular forms of epithelia are far more prevalent in the pelves and calices than in the bladder, and are well adapted for a diagnosis.

All epithelia change to a certain degree in the urine, more especially the cuboidal, which are originally angular polyhedral formations; by the imbibition of the watery constituent of the urine, they swell and assume a more or less regular, even perfectly spherical, form. This change affects all epithelia alike, and the size of the spheres is sufficient for a diagnosis of their previous location.

In the vagina and bladder, where the epithelia are large, the difference between the flat, cuboidal, and columnar varieties is naturally most marked, while in the pelves, ureters, urethra, and cervical portions of the uterus it is not so pronounced. In the prostate gland the simple epithelial lining is usually cuboidal, though sometimes columnar, while in the ducts of the prostate gland and the seminal vesicles it is columnar only. In the ejaculatory ducts, as well as in the mucosa of the uterus, ciliated columnar epithelia are present, though in the urine the cilia break off easily and may not be seen. In the uriniferous tubules of the kidney the simple epithelial lining varies in different portions, being partly flat, partly cuboidal, and partly columnar; the flat and cuboidal epithelia cannot be distinguished, while the columnar variety is well marked.

In every urine flat, horny epithelia from the genitals—the prepuce in the male, and the clitoris and labia in the female—may be found, and are called epidermal scales (see Fig. 49). They have a jagged contour, are of a rather high refraction, and do not contain a nucleus, but are frequently studded with dirt particles and fat globules. In addition, their granulation if any is present at all, which is rarely the case—is extremely pale, and they appear more or less shrivelled. They vary in size and shape considerably, and must not be mistaken for true epithelia or crystals of incomplete triple phosphates, which latter they sometimes resemble more pronouncedly than the former.

In attempting to diagnose the sources of the different epithelia, it must be remembered that nothing but size will positively differentiate

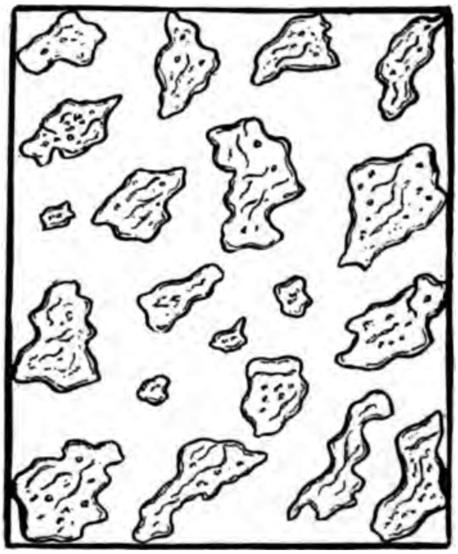

FIG. 49.—EPIDERMAL SCALES (× 500).

them, and that a small number of epithelia may be found, the source of which cannot be told positively; the larger number, however, are absolutely characteristic.

The epithelia found in the urine may be divided into: First, those common to both sexes; second, those found only in the male; and third, those found only in the female.

Epithelia Common to Both Sexes. — The epithelia found in both sexes are those from the bladder, the pelves of the kidneys, the ureters, and the uriniferous tubules of the kidneys. The urethral epithelia are also the same in both sexes, but are most common in the male.

Epithelia from the Bladder (see Fig. 50).—The epithelia from the bladder are of three distinct varieties and are easily recognizable; these are flat epithelia from the upper layers, cuboidal from the middle layers, and columnar from the deepest layer. Flat epithelia may be seen both in front view and edgewise, when they may appear more or less folded. A small number of these epithelia, without the presence of pus-corpuscles, may be seen in every normal urine. They have no significance whatever, since the flat epithelia continually desquamate in health, though in a small amount only. As soon as they occur with pus-corpuscles and with cuboidal epithelia, they have a pathological significance. These flat epithelia may be seen either singly or in clusters of varying size. Although

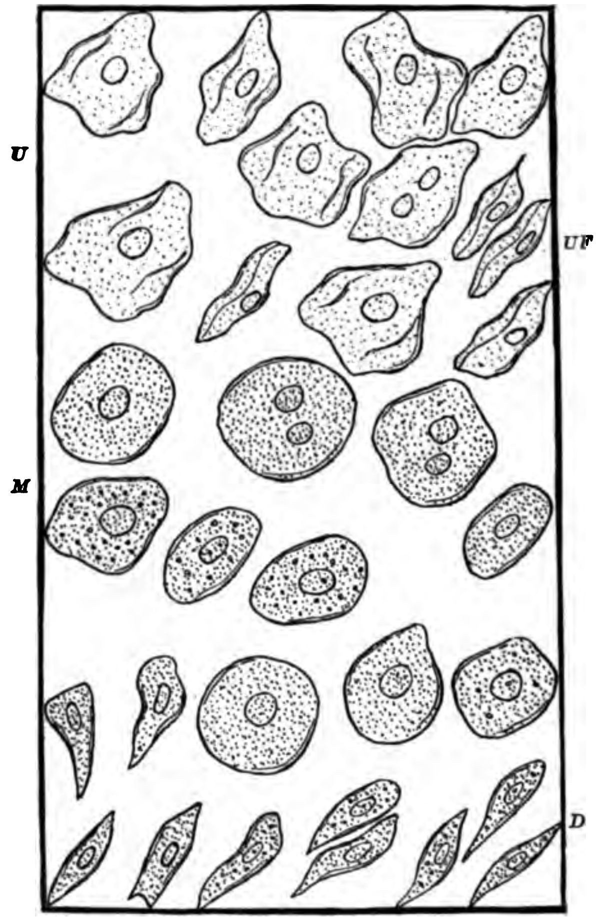

FIG. 50.—EPITHELIA FROM THE BLADDER (× 500).
U, Upper layers; *UF*, upper layers, folded; *M*, middle layers; *D*, deepest layer.

the size of these epithelia is distinctly smaller than that of the epithelia from the upper layers of the vagina, a small number may occasionally be found, of almost the same size as the latter, derived from the neck of the bladder, near the prostate gland. Their number, together with the size of the cuboidal epithelia and the fact of their not containing bacteria, is as a rule sufficient to clear up the diagnosis.

Cuboidal epithelia from the middle layers are never found in normal urine; they may be scanty or numerous. When cuboidal epithelia are present in moderate or large numbers, with many flat epithelia from the upper layers, the diagnosis of an acute process can be made. If, on the other hand, the upper layers are scanty or entirely absent, the process is a chronic one. Whenever fresh exacerbations of an old process set in the flat epithelia become more numerous.

Columnar epithelia from the deepest layer of the bladder are found only in the severer processes, such as intense inflammation, ulceration, hemorrhage, and tumors. Care must be taken not to mistake the folded upper layers for these more coarsely granular and more highly refractive epithelia—those from the upper layers being paler and finely granular.

Mention should here be made of an occurrence, which, though it may be found in the epithelia of any organ, is most pronounced in the larger cuboidal epithelia of the bladder. In different epithelia from the middle layers, a number of nuclei or even newly formed, so-called endogenous pus-corpuscles will be found. Their number varies from two to four, five, or even more. That pus-corpuscles are formed within epithelia can be easily observed. A few of these new-formations can often be seen in different inflammations, but larger numbers will be found in the epithelia only after a long-continued irritation through some pressure, usually from the outside. Such endogenous new-formations are seen in cases of hypertrophied prostate gland, undoubtedly caused by pressure of that organ upon the bladder, as well as in different exudations behind the bladder, such as a parametritic exudate or a tumor in the wall or vicinity of the bladder.

All cuboidal and columnar epithelia may contain a varying number of secondarily developed, glistening fat-granules and -globules similar to those seen in the pus-corpuscles. This is invariably an indication that the process has lasted for some time and is not an acute one. A large number of these globules always indicates a chronic process.

Epithelia from Pelvis of Kidney (see Fig. 51).—In the pelves of the kidneys the epithelia also vary considerably in shape, being partly globular, but mostly irregular. They are smaller than those from the bladder, but larger than those from the ureters, the epithelia from which latter are almost always present with those from the pelves. The majority of the pelvic epithelia are caudate, pear-shaped, or lenticular, though they are sometimes quite irregular; the regular, cuboidal shapes, smaller than those from the bladder, being less numerous. The epithelia are frequently seen with uric-acid gravel, which causes an irritation or inflammation of the pelvis.

Epithelia from the Ureters.—Epithelia from the ureters are rarely found alone, but usually with those from the pelvis. Their characteristic shape in the urine in most cases is round, globular, or slightly irregular,

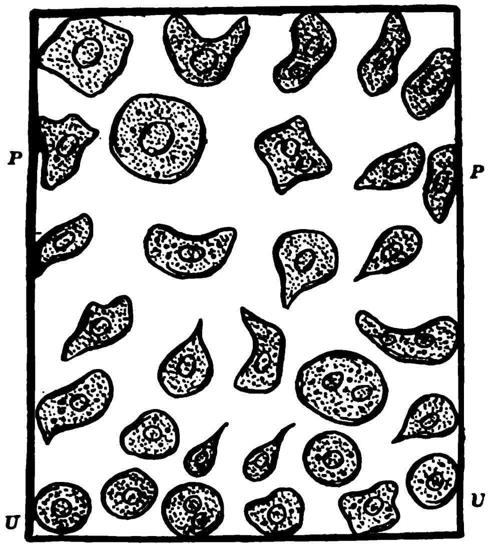

FIG. 51.—EPITHELIA FROM PELVIS OF KIDNEY AND URETER (× 500).
P, Pelvis of kidney; *U*, ureter.

being distinctly smaller than those from the pelvis. They cannot be differentiated from the epithelia of the prostate gland, which they closely resemble. Their number in the urine is, as a rule, small; and the fact of their being associated with epithelia from the kidney and pelvis of kidney makes their diagnosis easy. Occasionally small columnar epithelia from the deepest layer are seen. These are caudate or pear-shaped and are found in deep-seated processes, such as ulcerations due to impacted calculi or tubercular lesions. In traumatism, which may be due to ureteral catheterization, they are not rarely present in the urine.

Epithelia from the Uriniferous Tubules of Kidneys (see Fig. 52).—Epithelia from the uriniferous tubules are the most important of all the epithelia found in the urine and those most frequently overlooked. Whenever they are present in the urine, with pus-corpuscles, even when no casts whatever can be found, the diagnosis of a pathological process in the kidney is certain, since they are never seen normally in urine. Two distinct forms are found: the cuboidal from the convoluted tubules, and the columnar from the straight collecting tubules. These epithelia are distinctly smaller than either those from the pelvis of the kidney or the ureter in the same case, though their sizes vary to a certain degree in different cases. They are round, globular, or slightly irregular.

In every case examined the first step is to look for pus-corpuscles, which are known to be small in some individuals and comparatively large in others, and are usually the smallest granular corpuscles seen. They may vary in size in the same case, but to a slight degree only. As soon as these are decided upon, the next step is to determine whether bodies distinctly larger than these are present. If such bodies, about one-third larger than pus-corpuscles, are found in at least moderate numbers, we can be certain that they are epithelia from the convoluted and narrow tubules of the kidney. The presence or absence of a nucleus has no significance whatever, although such a nucleus is usually found in the kidney epithelia, but may be invisible in the pus-corpuscles. The relation between the size of the pus-corpuscles and that of the epithelia from the convoluted tubules is always the same; that is, the latter are about one-

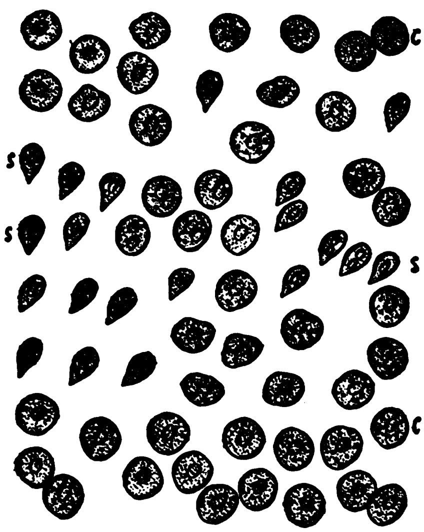

FIG. 52.—EPITHELIA FROM URINIFEROUS TUBULES OF KIDNEYS (× 500).
C, Convoluted tubules; *S*, straight collecting tubules.

third larger in diameter than the former. If the pus-corpuscles happen to be small in the case examined, the kidney epithelia will be small; but if large, the epithelia will be large.

The comparative sizes of the different smaller formations found in the urine are illustrated in Fig. 53. The smallest corpuscles with double contour, and which are not granular, are the red blood-corpuscles; the next in size, being the smallest granular corpuscles, are the pus-corpuscles; then follow the smallest epithelia found in urine, one-third larger than the pus-corpuscles—the epithelia from the convoluted tubules of the kidney. Finally, the next larger epithelia are shown, always about twice the

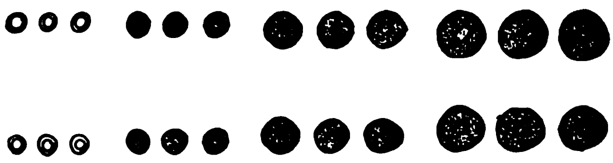

FIG. 53.—COMPARATIVE SIZES OF CORPUSCLES AND EPITHELIA (× 500).

diameter of the pus-corpuscles, which are either those from the ureters or the prostate gland, between which no difference can be noticed. If this relationship is kept in mind, no mistake can be made, though it must be remembered that when an individual small formation is found, the diagnosis cannot be made positively until compared with the pus-corpuscles.

Besides the cuboidal epithelia, columnar epithelia from the straight collecting tubules are sometimes found. The latter are, as a rule, not as abundant as the former, and are almost invariably seen in larger numbers in the severer cases of nephritis only. Their size, as compared with that of the cuboidal epithelia, is about the same, they being narrower, but elongated. In very acute cases of nephritis clusters of kidney epithelia, as well as cast-like tubes of epithelia, though not necessarily true casts, may be found.

Although it is the usual custom to rely entirely upon the presence of casts in the urine before making the diagnosis of a nephritis, it will be found that casts are frequently absent, even in pronounced cases of kidney inflammations, as, for instance, in catarrhal or interstitial nephritis; and that even in cirrhosis of the kidney, casts are, as a rule, entirely absent, or, if present, are extremely scanty. If care is taken to look for epithelia about one-third larger than pus-corpuscles, the diagnosis of a nephritis can be made in many cases which are otherwise overlooked, even though a small or even moderate amount of albumin be present in the urine. Too much stress cannot be laid upon this fact, as, in many cases where the clinical symptoms undoubtedly point to a nephritis, the diagnosis is abandoned because no casts are found. This variety of nephritis is much more common than is usually supposed, though in most cases of a milder character than the parenchymatous variety, and it may often last for a number of years without being detected.

The diagnosis of epithelia from the upper urinary tract has of late years been simplified by ureteral catheterization. Whenever such urines, obtained by means of the ureteral catheter, are examined, where the presence of epithelia from the bladder or the genital tract can positively be excluded, only those epithelia which have been described as being derived from the ureter, pelvis of kidney, and uriniferous tubules are found.

Epithelia Found in Urine of Male.—The epithelia found in the urine of the male are those from the urethra, the prostate gland and its duct, the seminal vesicles, and the ejaculatory duct.

Epithelia from Urethra (see Fig. 54).—The epithelia from the urethra vary considerably in size and shape, being partly flat, partly cuboidal, and partly columnar, and in most cases are comparatively large and irregular, so that they can be easily diagnosed. The larger irregular, partly flat, partly cuboidal epithelia are seen in milder inflammations, such as the first stages of catarrhal or gonorrhœal inflammations; the irregular columnar or cylindrical epithelia occur only in deeply seated inflammations or ulcerations, which often lead to the formation of a stricture.

Epithelia from Prostate Gland (see Fig. 55).—The epithelia from the prostate gland are partly cuboidal and partly columnar, the latter orig-

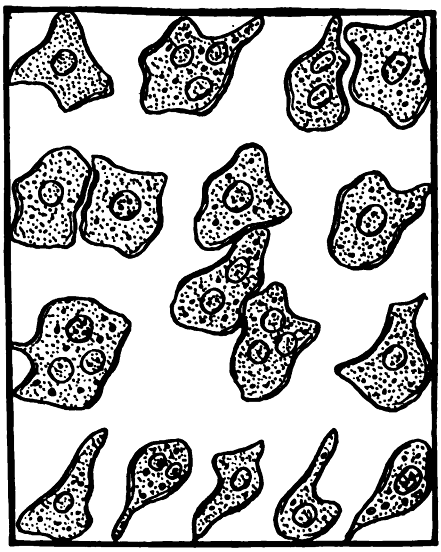

FIG. 54.—EPITHELIA FROM URETHRA (× 500).

inating both in the alveoli and the excretory ducts of the gland. The cuboidal epithelia are of exactly the same size as the cuboidal epithelia from the ureters, being about twice as large as the pus-corpuscles in every case, and distinctly larger than those from the convoluted tubules of the kidney. When epithelia of this size are seen in a given case, care must be observed to take the relative numbers of these, as well as of those from the convoluted tubules and the pelvis of the kidney, into consideration before reaching a positive diagnosis. For instance, if they are present in large numbers, while those from the kidneys and pelves are entirely ab-

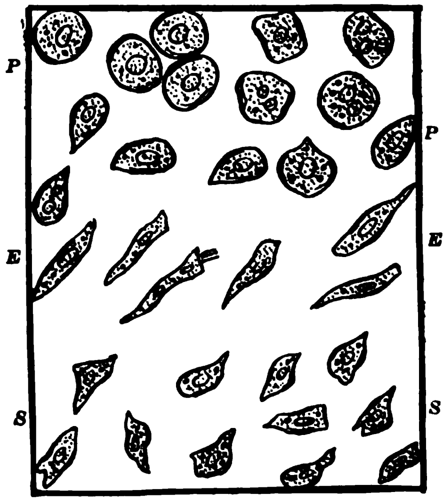

FIG. 55.—EPITHELIA FROM PROSTATE GLAND, SEMINAL VESICLES, AND EJACULATORY DUCTS (× 500).

P, Prostate gland and its ducts; *E*, ejaculatory ducts; *S*, seminal vesicles.

sent or seen in small numbers only, they are undoubtedly prostatic. The clinical history, if known, will, of course, clear up this point still further.

The columnar epithelia, partly from the ducts of the gland, which are distinctly larger than those from the straight collecting tubules of the kidney, are rarely absent in pathological processes of the prostate gland, and will render the diagnosis plain, since columnar epithelia from the ureters, which they resemble, are not frequently seen, and, when present, are usually found in small numbers only. The latter also are more caudate than the former.

In many cases of posterior urethritis associated with prostatitis, groups of round, oval, or slightly irregular epithelia are found. These are larger than the prostatic epithelia just described, resembling in size the cuboidal epithelia from the pelvis of the kidney, but are pale, usually finely granular, with their nuclei frequently indistinct. They are hydropic, and may be derived from both the prostate gland and the prostatic portion of the urethra.

Mention should be made here of the fact that in rarer cases pale, concentric formations of varying sizes are found with the prostatic epithelia. These are the so-called prostatic concretions, colloid or amyloid corpuscles of the prostate gland (see Fig. 56). They are irregular, partly oval, partly angular bodies, which have a high refraction and a more or less pronounced concentric striation, frequently with an irregular central nucleus. Their number seems to be augmented in some cases of hypertrophy of the gland.

Epithelia from Seminal Vesicles.—Epithelia from the seminal vesicles (see Fig. 55) are frequently associated with those from the prostate gland. Their presence in urine with pus-corpuscles indicates an inflammation or suppuration in the vesicles. These epithelia are always columnar and non-ciliated. They are more or less irregular, either of the same size or slightly larger than the columnar epithelia from the prostate, and in the organ contain yellow pigment. The pigment is sometimes, but not always, seen in the epithelia in urine.

Epithelia from Ejaculatory Ducts.—Epithelia from the ejaculatory ducts may also be found in the urine. They are of the columnar ciliated

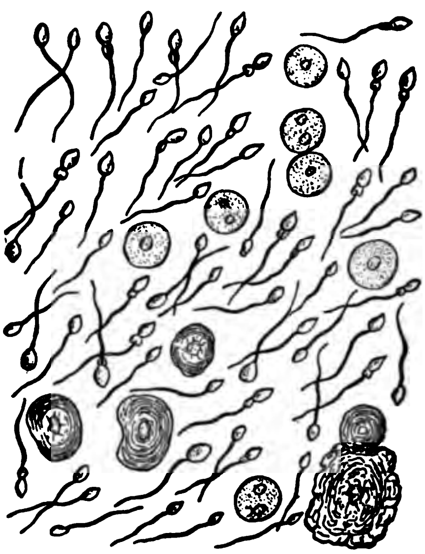

FIG. 56.—SPERMA AS FOUND IN URINE (× 500).

variety, and perfectly characteristic. The cilia are not always seen, since they break off easily and become lost; but delicate parallel rods in the interior of the epithelia, near their basal surface, may then indicate that the epithelia were originally ciliated. When no cilia or rods are found, their size alone will usually be sufficient for a diagnosis, as they are smaller and considerably narrower than those from the bladder.

Sperma.—Not infrequently sperma, the characteristic ingredients of which are the spermatozoa, is found in urine, normally as well as pathologically. This will be the case after sexual intercourse, as well as after emissions, and in spermatorrhœa, which latter can best be diagnosed from the almost constant presence of sperma in urine, especially the first urine voided in the morning. When sperma is found in small amount only, the appearance of the urine is not changed; but when present in large amount, cloudy, flaky deposits are seen, which, when examined, prove to be sperma.

In urine the positive diagnosis of sperma can only be made when spermatozoa are found, though prostatic epithelia, and occasionally spermatic concretions, may be present (see Fig. 56). The other ingredients of sperma, such as the sperma crystals, are rarely seen in urine.

Spermatozoa, which are about $\frac{1}{500}$ or $\frac{1}{600}$ of an inch long, consist of a flattened, oval, or pear-shaped head, a small cylindrical middle portion or neck, which, however, is not always seen, and a long, wavy, tapering tail, considerably broader at the head than at the end. In perfectly fresh urine a slight motion of the spermatozoa may be visible for a short time, but disappears very soon. They are extremely resistant toward chemical reagents, and may be found well preserved in urine after days, even when it is strongly alkaline.

The number of spermatozoa in urine varies greatly. Under normal conditions the spermatozoa are rarely abundant, while in cases of spermatorrhœa they are usually quite numerous and may be present in very large numbers. In cases of spermatocystitis or seminal vesiculitis they are frequently seen, and many of them will be found changed, the head gradually enlarging, becoming more round and often granular. It is not unusual for the head to assume the size of a pus-corpuscle, which it may resemble to such a degree that it is impossible to differentiate it from the latter; in appearance, it is like a pus-corpuscle with a tail. In these cases pus-corpuscles, epithelia from the prostate gland, from the seminal vesicles, and frequently also from the ejaculatory ducts will be present.

Urethral and Gleet-Threads.—Although no distinction should be made between urethral and gleet-threads or filaments (the latter originating in the urethra), there are cases in which men who have never suffered from gonorrhœa will void small, transparent mucus-threads or filaments with the first morning urine. These are always scanty, and consist of nothing but mucus, both threads and corpuscles, together with the larger, flat, superficial urethral epithelia. These masses are conglomerations of mucus in the urethra, and are not pathological.

On the other hand, we find in the urine of persons who have suffered from gonorrhœa, at one time or another, either only a short time previously or many years before, a varying number of filaments, which differ in size and may appear either perfectly transparent or more or less opaque. These are the regular gleet-threads (see Fig. 57).

It is not uncommon to find such filaments accidentally in the urine of persons who, though they suffered from gonorrhœa a long time previously, have not noticed any symptoms for years. In these cases they are, of course, small and scanty. More frequently are they found in those cases of chronic gonorrhœa in which slight symptoms, such as a moisture at the orifice of the urethra or an adhesion of the lips of the

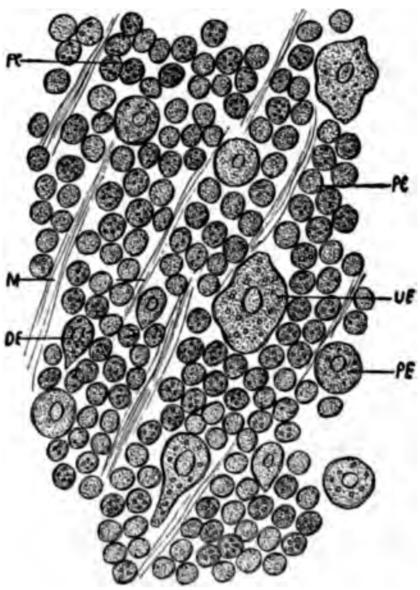

FIG. 57.—GLEET-THREADS (× 500).
PC, Pus-corpuscles; *M*, mucus-fibres; *PE*, epithelium from the prostate gland; *DE*, epithelium from the ducts of the prostate gland; *UE*, epithelium from the urethra.

meatus in the morning, with subsequent discharge of a minute drop of either mucous or muco-purulent fluid, are present. The number of filaments in cases of this kind is at times very large. Fortunately, gonococci are not found in all these cases, but may be entirely absent in the larger number, and repeated careful examinations will fail to find them.

Regular gleet-threads consist of mucus, pus-corpuscles (the latter usually abundant in the more pronounced cases), and a varying number of epithelia from the urethra and the prostate gland; sometimes, also, from the neck of the bladder. The larger number of pus-corpuscles, as well as most of the epithelia, will be found studded with fat-globules and -granules, which latter are not infrequently seen in smaller or larger groups upon and between the mucus, outside of the pus-corpuscles and epithelia. The more chronic the case, the more numerous are the fat-globules. The appearance of such so-called gleet-threads under the microscope is always

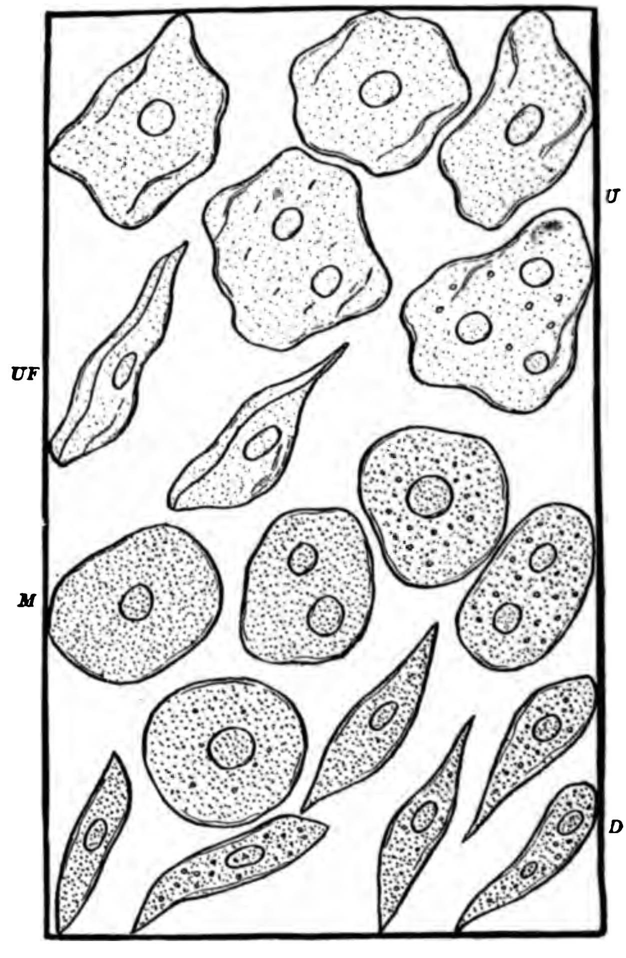

FIG. 58.—EPITHELIA FROM THE VAGINA (× 500).
U, Upper layers; *UF*, upper layers folded; *M*, middle layers; *D*, deepest layer.

perfectly characteristic, though the name is misleading, since, when they are large, a number of fields can be found crowded with pus-corpuscles, mucus, and epithelia not in the least resembling a thread.

The more severe the case, the more abundant are the pus-corpuscles, and care is necessary in such cases not to make an error in the diagnosis, which would be easy when the presence of gleet-threads is not suspected. A wrong diagnosis of an abscess might thus be made, although such a diagnosis is never justified without the presence of a number of connective-tissue shreds, which are never seen here. In the milder forms the mucus is abundant, and the pus-corpuscles mixed with it often change and assume various irregular shapes, the spindle shape being frequent. It is impossible to judge of the chronicity of a case from these, as has been claimed. Again, the pus-corpuscles may swell and become hydropic, or the cover glass may have been accidentally pressed in mounting the specimen, either of which is sufficient to change the appearance of the pus-corpuscles. Spermatozoa may at times be found mixed with the gleet-threads, but will, of course, not affect the diagnosis in any form.

Epithelia Found in Urine of Female.—The epithelia found in the urine of the female are those from the vagina, the Bartholinian gland, the cervix of the uterus, and the mucosa of the uterus.

Epithelia from Vagina.—The epithelia from the vagina are the largest found in the urine; those from the upper layers are flat, those from the middle layers are cuboidal, and those from the deepest layer are columnar (see Fig. 58).

The flat epithelia are present in varying numbers in most female urines, and when found alone have no significance, since they continually desquamate in health. When leucorrhœa is present, as is almost always the case, in a small degree, in healthy women who have borne children, their number is considerably augmented. They may be found singly or in variously sized clusters, and are always large, irregular, and usually studded with bacteria—both cocci and bacilli. They frequently contain large fat-globules, which, of course, have here no significance; they are often seen folded or edgewise, when they are narrow but irregular, and cannot be mistaken for columnar epithelia. Their granulation is fine, and the epithelia, therefore, pale.

The cuboidal epithelia from the middle layers are abundant in inflammations of the vagina. They are considerably larger than those from the bladder, have one or more nuclei, and in chronic inflammations contain fat-granules and -globules. These are also found in clusters of considerable size.

The columnar epithelia from the deepest layer, much larger than those from the bladder, are seen only in intense, deep-seated inflammations or ulcerations, where they may sometimes be found in large numbers.

Smegma.—Of common occurrence in the urine of the female are clusters of epidermal scales, so-called smegma, partly from the clitoris, partly from the labia, or from the vagina. Smegma may also be found in small amount in the male, from the prepuce, but here it is not so common nor seen in such enormous masses as in the female (see Fig. 59).

Smegma consists of closely packed masses of variously sized epidermal scales filled to a greater or less degree with bacteria—both cocci and ba-

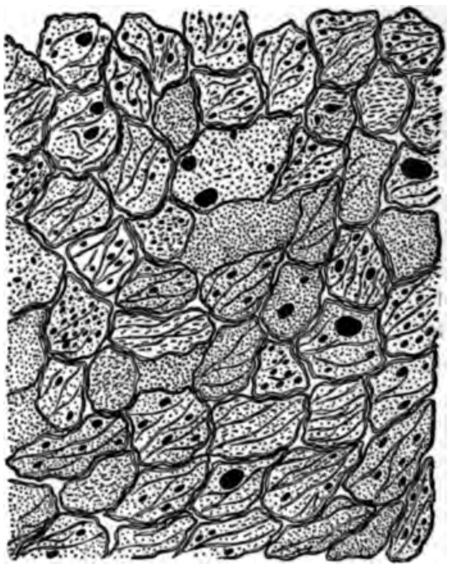

FIG. 59.—SMEGMA FROM THE CLITORIS (× 450).

cilli—and also with extraneous fat-globules, as well as particles of dirt. The individual scales, as before said, are never nucleated and rarely granular, but appear shrunken. Such masses, which have been seen to cover an entire field of the microscope, are highly refractive, and when large can be seen with the naked eye.

Epithelia from Bartholinian Gland (see Fig. 60).—The epithelia from the Bartholinian gland resemble in size the round or slightly irregular epithelia from the prostate gland in the male, being about twice the diameter of pus-corpuscles. They are frequently present when the vaginal epithelia are found in moderate or large quantities.

Epithelia from Cervix Uteri.—Epithelia from the cervical portion of the uterus are partly flat, partly cuboidal, and partly columnar, and quite large, though considerably smaller than those from the vagina, and always more irregular. These epithelia may be characteristic, but they sometimes so resemble the irregular epithelia from the urethra as to be difficult of differentiation. The latter are found in the female as well as the male, though generally in smaller numbers.

Epithelia from Mucosa Uteri. — Epithelia from the mucosa of the uterus, indicating a catarrhal endometritis, are also not rare in the urine. They are delicate, columnar, ciliated formations, smaller than those described as being derived from the ejaculatory ducts. The cilia on the surface of these epithelia are frequently well marked, and as many as three or four may be found; occasionally, however, they are broken off. With them we may see ciliated pus-corpuscles, which arise from the epithelia, and cannot come from any other locality than the uterus. In freshly voided urine the cilia from both these formations may be seen in waving motion.

If the epithelia just described are carefully studied, we will soon become convinced that the formations from the different organs of the genito-urinary tract can undoubtedly be differentiated, and that diagnoses of the different lesions can be made with great certainty. In every

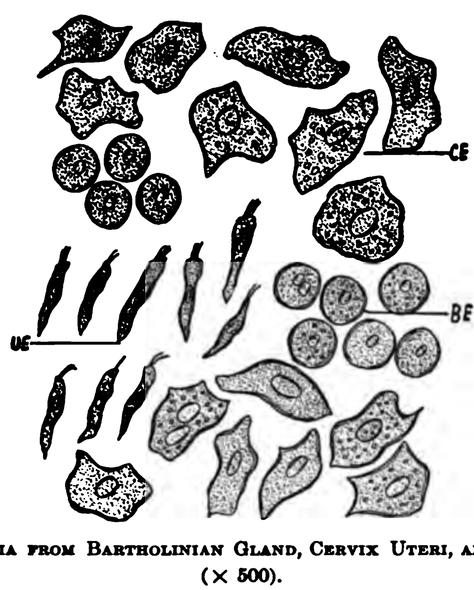

FIG. 60.—EPITHELIA FROM BARTHOLINIAN GLAND, CERVIX UTERI, AND MUCOSA UTERI (× 500).
BE, Bartholinian gland; *CE*, cervix uteri; *UE*, mucosa uteri.

case in which at least a moderate number of epithelia is found in the urine, most of these are characteristic of the organ from which they are derived. There will, of course, always be a few, the origin of which must remain doubtful, but these are not sufficiently numerous to cause errors. The more cases we examine, the more convinced we will become of this fact. The clinical history of the case will bear out the microscopical diagnosis every time, and frequently the microscope gives the first indication of some pathological condition which has as yet escaped detection, but which sooner or later is bound to give clinical symptoms. In no organ is this more pronounced than in the kidney, where mild cases of nephritis, which unfortunately escape detection for months or years, may be present, until suddenly the pronounced symptoms of a chronic nephritis or a cirrhosis of the kidney develop. Conscientious examination of the urine for kidney epithelia and pus corpuscles will often repay the physician in cases where, although he has found a trace of albumin, he will banish from his mind all idea of an inflammation of the kidneys because no casts are present.

CHAPTER XII.

MUCUS AND CONNECTIVE TISSUE.

I. *MUCUS.*

Mucus is found in small amount in every normal urine, being, as a rule, more abundant in females. It appears in the form of threads and corpuscles, and is a normal physiological product of the epithelia (see Fig. 61).

Mucus-threads are finely striated, pale, often scarcely perceptible strings of different sizes. In normal urine they are always small; but in inflammations, especially those of the genital tract, may assume large proportions. The strings are made up of pale, more or less parallel fibres, and when large may branch in different directions.

Besides threads, mucus-corpuscles are of frequent occurrence. These corpuscles vary in size from that of a pus-corpuscle to that of larger epithelia; are pale, more or less irregular in outline, always finely granular, and non-nucleated. They are easily distinguished from pus-corpuscles by their greatly varying sizes, pale appearance, and absence of a nucleus, which latter is seen in finely granular pus-corpuscles.

Mucus-threads not infrequently appear in the form of delicate, striated formations, resembling casts, the so-called cylindroids or mucus-casts (see Fig. 62). Although at times greatly resembling hyaline casts in their outline, they can usually be distinguished from them by their irregular contours, their tapering ends, and their more or less striated interior, since they are nothing but conglomerations of mucus-fibres. They may be quite long and are often twisted and folded. They may be found whenever mucus is present in larger amounts, and may be derived from any portion of the genito-urinary tract. They undoubtedly have no further significance than mucus in general.

Mucus is greatly augmented in all inflammatory conditions, but more especially in inflammations of the bladder and the genital organs, such as the urethra, prostate gland, and vagina. In the latter, mucus-threads are often large, cylindrical, and twisted, and may be perceptible to the naked eye. The so-called gleet-threads are nothing but conglomerations of mucus, in which large numbers of pus-corpuscles and epithelia are embedded. Irritation of the urinary tract, due to highly acid urine, containing uric acid and sodium urate, increases the amount of mucus, and, the urates being precipitated upon it, the stringy masses become more easily perceptible. Fat-granules and -globules, so frequently found in the urine, may also conglomerate upon mucus-threads and so-called cylindroids.

In chronic inflammations of the bladder the urine appears ropy, on

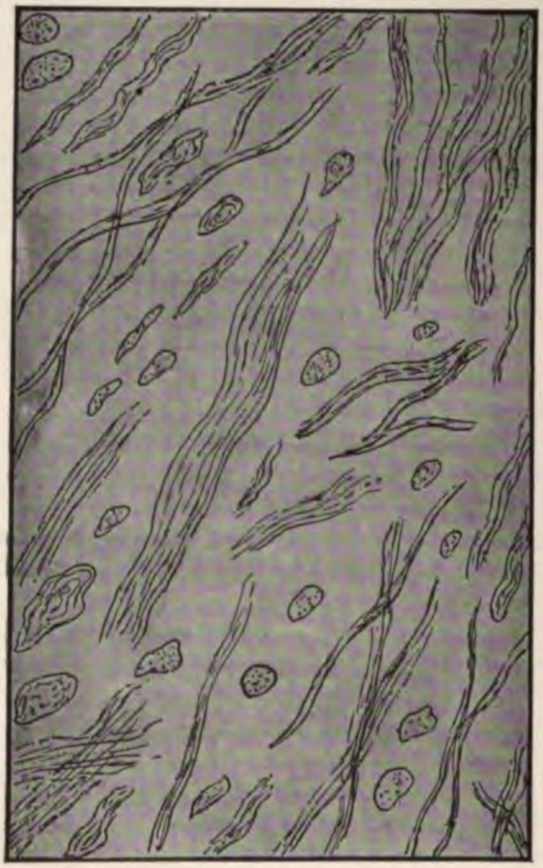

FIG. 61.—MUCUS-THREADS AND -CORPUSCLES (× 500).

account of the abundance of mucus. Simple irritation of the sexual organs is sufficient to increase the amount of mucus, and if sperma is mixed with the urine its mucous constituents appear as pale, flaky masses entangled with spermatozoa.

Finally, an increased amount of mucus may be seen in the urine in different febrile conditions, without any inflammation in the urinary tract; and in acute contagious diseases, such as scarlet fever, it frequently appears as a precursor of a nephritis.

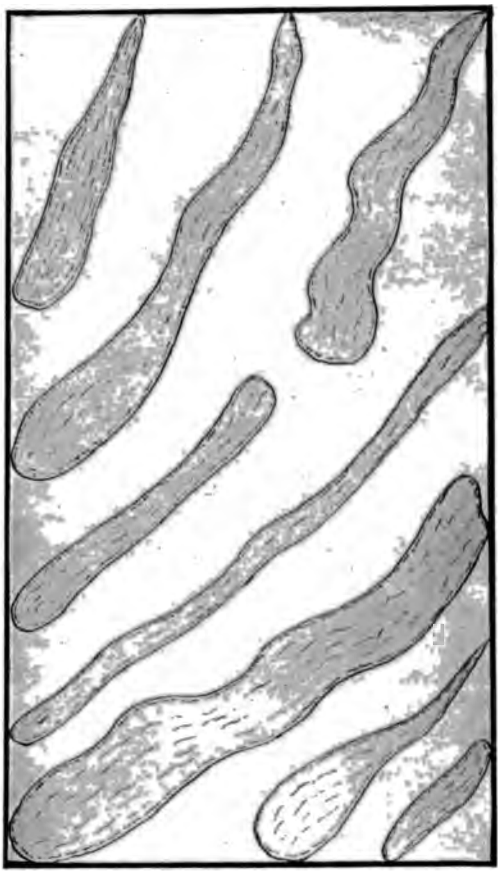

FIG. 62.—MUCUS-CASTS OR CYLINDROIDS (× 500).

II. CONNECTIVE TISSUE.

As all the organs containing epithelia also contain connective tissue, it is evident that this formation can frequently be found in the urine, though only in the more intense, deeper-seated pathological processes. Its occurrence has, however, been entirely overlooked, except in the rare cases in which particles of tumors, especially from cancers, have been found in the urine. That connective-tissue shreds are of comparatively common occurrence was first pointed out by Carl Heitzmann, who described their appearance under a number of different conditions. The reason for their being overlooked seems to be, partly, that in many cases they are small, though easily seen, and partly that they have been mistaken for mucus-strings or extraneous substances, such as linen and cotton fibres.

FIG. 63.—CONNECTIVE-TISSUE SHREDS (× 500).

Connective-tissue shreds (see Fig. 63) vary in size, and are made up of wavy, moderately refractive fibres, the individual fibres being rarely single, but conglomerated in the form of small, irregular bundles, which again form larger bundles. These bundles, then, are always fibrillary and frequently finely granular, sometimes even containing formations resembling nuclei—the connective-tissue corpuscles. They may be so small and delicate as entirely to escape detection with a magnifying power of less than 500 diameters, or so large as to cover half or even the entire length of a field, and of varying thickness. They are easily differentiated from mucus-threads by their moderate refraction and their wavy, irregular fibres, in contradistinction to the pale appearance and more or less regular fibres of mucus, which frequently run in a parallel direction for a considerable distance. On the other hand, linen fibres, or, rather, the smaller fibrillæ of linen, with which they might also be confounded, are of a still higher refraction, and are coarser, the individual fibrillæ being split up in an entirely different manner, and are never as wavy as the connective-tissue shreds.

The pathological conditions under which connective-tissue shreds are found may be divided into the following:

1. Ulceration.
2. Suppuration.
3. Hemorrhage.
4. Traumatism.
5. Tumors.
6. Hypertrophy of the prostate gland, with inflammation of that organ.
7. Stricture of the urethra.
8. Cirrhosis of the kidney.
9. Atrophy of the kidney.
10. In all other intense inflammatory processes, but in small amount only.

As an example of the latter, the croupous or parenchymatous inflammation of the kidney may be mentioned, in which, if it is at all severe, connective-tissue shreds will be found in small numbers.

1. *Ulceration.*—Ulcerative processes are quite common occurrences, and may be found in any part of the genito-urinary tract, but more especially in the bladder, pelvis of kidney, urethra, and vagina. In such ulcers the connective-tissue shreds are usually broad and numerous, pus-corpuscles are present in moderate or fairly large numbers, and the location of the ulcer can always be determined by the presence of the characteristic epithelia; these are abundant, and found not only from the more superficial, but also from the deeper layers. Besides these formations, the freshly voided urine contains variously sized conglomerations of cocci, in the form of zoöglœa masses, especially around the connective-tissue shreds, as well as small numbers of other bacteria.

2. *Suppuration.*—The presence of an abscess in any organ can be diagnosed when connective-tissue shreds in large numbers are seen with numerous pus-corpuscles and epithelia from the organ in which the abscess is situated, this being most frequently either the kidney, the pelvis

of the kidney, the prostate gland, or the seminal vesicles. In many cases we will also see pronounced endogenous new-formations in the epithelia of the neighboring organs, as the result of pressure upon that organ. An abscess of the prostate gland, for instance, may give endogenous new-formations in the epithelia of the bladder, as well as of the urethra. Large numbers of pus-corpuscles and epithelia alone, without the presence of connective-tissue shreds, are never sufficient to diagnose an abscess. As soon, however, as these shreds, showing a destructive process, are found, the diagnosis becomes plain. The connective-tissue shreds, although always quite numerous, may vary considerably in size.

3. *Hemorrhage.*—In hemorrhages of the genito-urinary tract, it is often quite difficult to find the epithelia showing their source—the more abundant the hemorrhage, the greater the difficulty. It sometimes requires hours to arrive at a definite conclusion, though a certain number of epithelia will always be found sooner or later. In all such cases connective-tissue shreds are present, but are occasionally quite scanty and small, except when the hemorrhage is due to a tumor. They have, as a rule, a yellowish tint, from the coloring matter of the blood. In hemorrhages red blood-corpuscles are very abundant, and white blood-corpuscles are generally seen in small numbers. Strings of fibrin, which must not be mistaken for connective tissue, are found in many of these cases, but pus-corpuscles are absent as long as there is no inflammation; if a hemorrhage intervenes upon an inflammation, all the evidences of the latter will, of course, be present with the former.

4. *Traumatism.*—Since traumatism, due to various causes, is frequently accompanied by hemorrhages or even ulcerations, the features would be those above given. There are, however, cases in which the injury does not cause a pronounced hemorrhage, yet the destructive process to the tissue is sufficient for connective-tissue shreds to appear in the urine, with but a few red blood-corpuscles. Among these may be mentioned slight injuries, due to the passage of a small amount of gravel; injury to the ureter, due to the passage of the ureteral catheter, which may be quite extensive; mechanical injury of the orifice of the vagina, due to masturbation; or injuries of the cervix uteri. In mechanical injuries, such as are caused by masturbation, vaginal epithelia from all three layers are found, together with a large number of epidermal scales from the labia, usually containing fat-globules, epithelia from the Bartholinian gland, a few pus-corpuscles, possibly a few red blood-corpuscles, and a small or moderate number of connective-tissue shreds. When the number of vaginal epithelia is not large, and connective-tissue shreds appear with numerous irregular epithelia from the cervix, with only a few pus-corpuscles, injuries around the cervix are indicated. Although of com-

paratively small practical importance, it must be known that connective-tissue shreds in the urine of females may be due to such causes.

5. *Tumors.*—In all tumors which can be diagnosed from the urine, such as papilloma, sarcoma, and cancer, connective-tissue shreds are the most important diagnostic features, without which the presence of a tumor cannot be positively diagnosed. Besides these, other evidences of a tumor are frequently found, though the connective-tissue shreds themselves may be characteristic enough for a diagnosis.

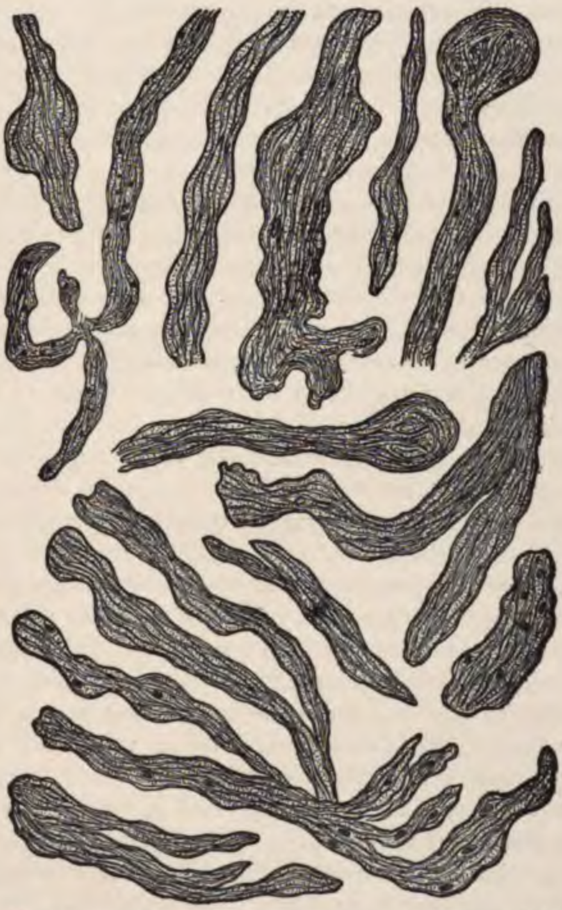

FIG. 64.—CONNECTIVE-TISSUE SHREDS FOUND IN TUMORS (× 500).

In papilloma such shreds are always large, very irregular, frequently branched, and often assume the shape of coils or knobs (see Fig. 64).

They are coarsely granular and may contain a number of inflammatory corpuscles. In rare cases blood-vessels in process of formation or fully developed may also be found in them. Besides these large masses, the regular connective-tissue shreds are also present in varying amount. A number of irregular, coarsely granular epithelia, the covering epithelia of the papilloma, will usually be seen in such cases, though they are not found *in situ* and are not of much value for a diagnosis.

In cancer of the bladder, especially villous or papillary, the connective-tissue shreds are occasionally still larger and more irregular, forming so-called cauliflower-like excrescences. They are infiltrated with inflammatory corpuscles, sometimes to a great degree, and often contain large cancer epithelia or even epithelial nests. Besides these shreds, such cases contain a varying number of epithelia about the size of those from the middle layers of the bladder, but extremely irregular, coarsely granular, and having numerous nuclei or pus-corpuscles in their interior—the so-called endogenous new-formations. In rarer cases variously sized cancer nests are also present. As a rule, both the connective-tissue shreds and the epithelia are seen crowded with fat-globules and -granules. The epithelia alone are never sufficient for a diagnosis, but as soon as the shreds just described are present the case becomes plain. That pus-corpuscles, bladder epithelia, and usually red blood-corpuscles are always found in these tumors is evident.

In sarcoma, which can develop in any organ of the genito-urinary tract and the location of which can be diagnosed according to the epithelia present, the connective-tissue shreds are frequently of very large size, but not characteristic. Here peculiar, glistening, coarsely granular, almost homogeneous corpuscles, smaller than pus-corpuscles but larger than red blood-corpuscles, are found in large numbers and variously sized groups.

6. *Hypertrophy of Prostate Gland.*—An enlargement of the prostate gland, when slight and unaccompanied by an inflammation, does not give connective-tissue shreds in the urine. As soon, however, as the hypertrophy becomes more pronounced and is accompanied by an inflammation, connective-tissue shreds, which may be small and scanty, appear in the urine, with pus-corpuscles and epithelia from the prostate gland and duct. Besides these features, we usually find the endogenous new-formations in the epithelia of the bladder or urethra, or both.

7. *Stricture of Urethra.*—A diagnosis of stricture of the urethra can also be made in a number of cases from an examination of the urine. This is of little practical value. In these cases cuboidal and columnar epithelia from the urethra, many of which have pronounced endogenous new-formations, are found with pus-corpuscles, red blood-corpuscles, and connective-tissue shreds in varying numbers. The features of an existing

hypertrophy of the prostate or a stricture of the urethra are not necessarily found in every specimen of urine.

8, 9. *Cirrhosis and Atrophy of Kidney.*—Every chronic interstitial nephritis sooner or later leads to cirrhosis of the kidney, and every chronic parenchymatous nephritis to atrophy of the kidney. In both of these affections connective-tissue shreds are also present, usually in small amount only in cirrhosis, but always in larger amount in atrophy. The features found in the urine in these diseases, besides connective-tissue shreds, are numerous and so constant that a diagnosis is simple.

10. That connective-tissue shreds may be also found in small numbers in every intense inflammation, is evident from what has been said. In tuberculosis of any organ of the genito-urinary tract, for instance, even if as yet unaccompanied by ulceration, a few shreds may be present in the urine. As soon as connective-tissue shreds, however small, are found, it becomes evident that the pathological process cannot be a mild one.

CHAPTER XIII.

TUBULAR CASTS.

TUBULAR casts were first carefully described as occurring in the tubules of the kidney and found in the urine by Henle in the year 1842, although they were probably seen a few years before that time by different observers. Many years later, in 1867, Rovida gave a thorough account of their nature and formation. Henle considered them to be coagulated fibrin, but the views concerning their origin have become greatly changed since that time. They were at one time considered to be products of secretion of the epithelia of the tubules, at another time to be transformed or disintegrated epithelia. Later on, the blood-vessels were supposed to be principally concerned in their production, at least in that of the hyaline casts, without any participation of the epithelia.

One of the older views was that casts are produced by the coagulation of an albuminous substance, the supposition being based upon the fact that the presence of casts in the urine depends upon the admixture of albumin, since they are found in conditions accompanied by albumin; and the more abundant the albumin, the more likely it is that casts are present. This view seems to be nearly correct. Casts are probably the products of an albuminous exudation from the blood-vessels, with the addition of the swollen and destroyed epithelia. In almost all cases where casts are present, albumin is found in moderate or large amount; but there are undoubtedly cases in which the amount of albumin is small, and, it is claimed, may even be entirely absent. The latter is, however, doubtful. The amount of albumin may be so small as to escape detection by the usual chemical methods employed; but, according to this view of their formation, it would seem that a small amount, at least, must be present in every case.

The appearance of casts in the urine is always of the highest diagnostic importance, and, if found in any amount, they indicate the presence of a croupous or parenchymatous nephritis, the more so the larger the accompanying amount of albumin. It is asserted that a mere hyperæmia of the kidneys may suffice to throw casts into the urine, and also that casts can be found in small numbers when the kidneys are perfectly intact. They have been described in cases of gastro-intestinal catarrh, in jaundice, acute and chronic anæmia, as well as in nervous affections of different kinds, without any accompanying inflammation of the kidneys. As they have been found in small numbers only in all such cases, it is a question whether true casts were seen, or only cylindroids, which at times it is almost impossible to distinguish from hyaline casts. In the majority of cases the presence of tube casts signifies the presence of a nephritis, but small numbers of hyaline casts may be found in renal congestion, unaccompanied by an inflammation.

In order to guard against any errors in the diagnosis, it is important to look for other abnormal features in the urine, when cast-like formations are seen; when none are found, such formations cannot be tube casts. It is not always easy to find casts in the urine, especially if only a few hyaline casts are present. The centrifuge throws them down readily, but unless the urine is centrifugalized for no more than three minutes, small numbers of casts may break up and escape detection. Again, cylindroids are more liable to be found in a centrifugalized specimen, and these may be mistaken for true hyaline casts. It is perhaps the safest plan to allow the urine to settle in a conical vessel for from six to twelve hours, provided it can be kept in a cool place, so that no putrefactive changes occur. Low magnifying powers are unreliable for the detection of casts, and a power of at least 400 diameters should always be used. Again, a number of specimens should be examined before positively determining as to the absence of casts.

Casts have been divided in many different ways, but perhaps the simplest is to divide them into *true casts* and *false* or *pseudo-casts*. The former alone denote the presence of a nephritis, while the latter are accidental formations.

I. *TRUE CASTS.*

True tube casts are of six varieties. These are:

1. Hyaline casts.
2. Epithelial casts.
3. Blood casts.
4. Granular casts.
5. Fatty casts.
6. Waxy casts.

Generally speaking, the first three varieties—hyaline, epithelial, and blood casts—are found in an *acute* parenchymatous or croupous nephritis, while the last three—*i.e.*, granular, fatty, and waxy casts—are found in a *chronic* parenchymatous inflammation of the kidney. In the first few weeks of the inflammation, granular and fatty casts rarely appear, waxy casts never; but as soon as the absolutely acute attack commences to subside and the inflammation assumes a more subacute form, granular casts, first in small, then in large numbers, are always seen, while the hyaline and epithelial casts are still abundant. Fatty and waxy casts are secondary products, and are rarely found until a nephritis has lasted for some time, although mixed epithelial and granular casts, commencing to become fatty, may be found a few weeks after the beginning of the inflammation. Exceptionally, as in phosphorus poisoning, fatty casts may be present at once.

All true casts may appear in three distinct sizes, according to the portion of the uriniferous tubules from which they originate. The narrowest casts are those formed in the narrow tubules, the next in size from the distal convoluted tubules, while the largest are always formed in the straight collecting tubules. Casts from the proximal convoluted tubules, those directly arising from the capsule of the tuft, never appear in the urine, since they cannot pass the narrow tubules.

Although not generally admitted, a great prognostic value undoubtedly attaches to the size of the casts. The mildest degrees of the disease are usually indicated by casts from the narrow tubules, and a small number of casts from the convoluted tubules. Not infrequently pedunculated casts are met with; that is, formations from the place of transition of the narrow tubules into the distal convoluted tubules. Casts from the convoluted tubules justify the diagnosis of parenchymatous nephritis in the cortical substance. Casts of all three sizes, the largest arising from the straight collecting tubules, permit of a conclusion of parenchymatous nephritis in the whole organ, and upon this condition a very unfavorable prognosis can be established.

Based upon these simple facts, a good or bad prognosis can be given in many cases where the clinical features are too obscure to be of any practical value; and not infrequently the bad prognosis, which has to be given on account of the presence of many large casts from the straight collecting tubules, and which does not at first seem justified by the scarcity of clinical symptoms, is soon borne out by the fatal end of the case.

Repeated examinations of urine, especially from a mixed twenty-four hours' voiding, should always be made before an opinion as to the prognosis of a case can be of any value. All the features, both chemical and microscopical, must invariably be taken into consideration. The determination of the amount of urea excreted in twenty-four hours, the total solids and the amount of albumin are of as much importance as the number and character of the pathological elements seen under the microscope.

1. *Hyaline Casts* (see Fig. 65).—Hyaline casts are pale, transparent formations of variable length, sometimes of considerable size, and not in-

frequently difficult of detection in the urine. Those from the convoluted and straight collecting tubules are usually more or less regular, though the latter may be very broad; those from the narrow tubules are occasionally tortuous or spiral, and at times exceedingly narrow and delicate. As a rule, these casts are absolutely structureless, but at times a pale granula-

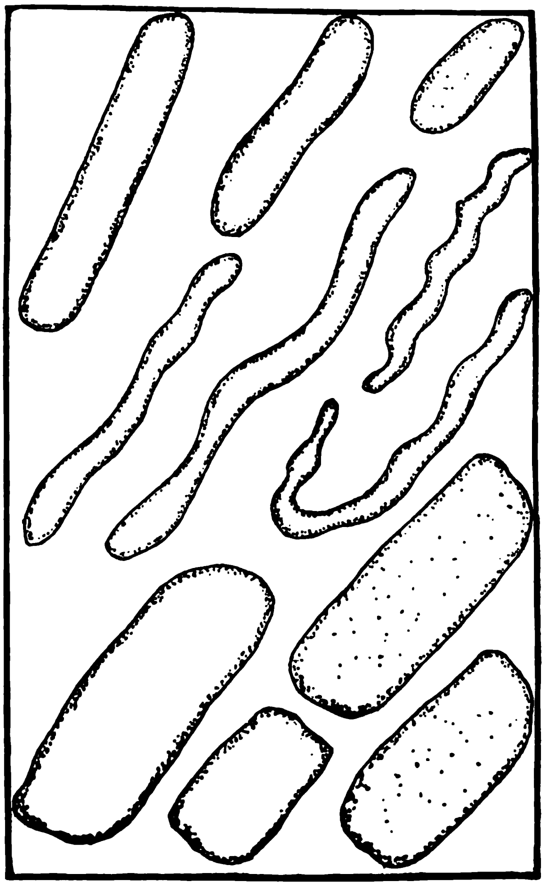

FIG. 65.—HYALINE CASTS (× 500).
Upper row, from convoluted tubules; middle row, from narrow tubules; lowest row, from straight collecting tubules.

tion is noticeable in them, though this is not sufficiently marked to allow of their classification as granular casts. Different formations, such as pus-corpuscles and fat-globules, may be seen upon them in small numbers, but are accidental and do not change the diagnosis. In rare cases these casts may appear more solid and of higher refraction, though their hyaline character is undoubted, and they must not be mistaken for waxy casts.

When very delicate and pale, it has been advised to color the casts by the addition of a drop of iodine-iodide of potash solution (iodine, 1 part; iodide of potash, 2 parts; water, 300 parts) upon the slide, which will stain them yellow and render them more distinct. This is rarely neces-

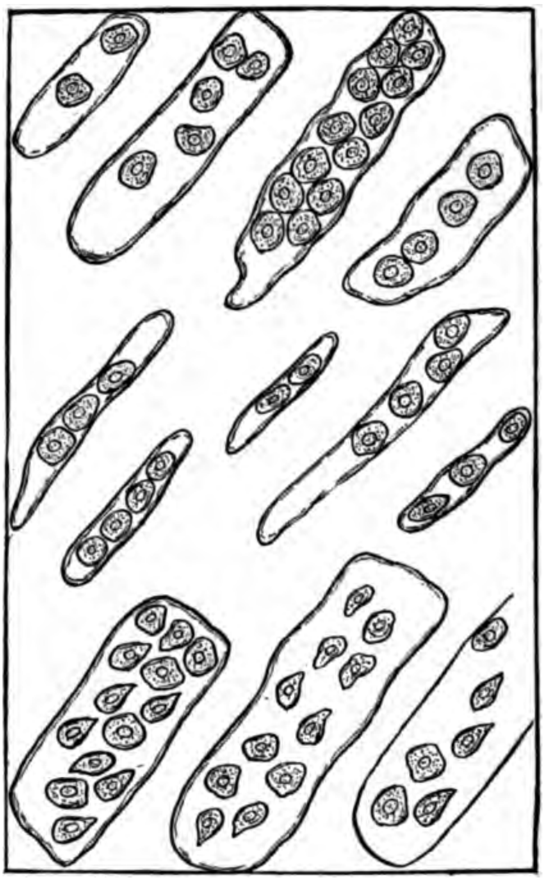

FIG. 66.—EPITHELIAL CASTS (× 500).
Upper row, from convoluted tubules; middle row, from narrow tubules; lowest row, from straight collecting tubules.

sary, since a sharp focus, perhaps with the light somewhat shaded, will bring them into view quite clearly. In a highly alkaline urine they are indistinct, and after a time seem to become lost completely.

2. *Epithelial Casts* (see Fig. 66).—True epithelial casts are hyaline

casts studded with epithelia. The desquamated epithelial tubes which are sometimes found in the urine, and represent solid masses of epithelia of varying length in the form of casts thrown off from the tubules, can hardly be called true casts, although they are usually classified as such.

Epithelial casts, when present, always denote an acute process; and the more pronounced it is, the larger is the number of these casts. They vary in size according to their origin, but are never as long as some hyaline casts and are usually quite regular. They are of a higher refraction than the former, and can be easily found. The number of epithelia seen upon these casts varies considerably. Sometimes no more than two, three, or four will be found upon a cast, while at other times the cast is completely filled with them, though still showing its structure plainly. Those from the convoluted and narrow tubules contain spherical or slightly irregular epithelia, while those from the straight collecting tubules usually also contain a number of columnar epithelia. Occasionally these casts are of a yellowish color with a slightly increased refracting power, owing to their imbibition of the coloring matter of the blood.

As long as the nephritis is acute, the epithelial casts will have the appearance just described, being more or less coarsely granular, but with the epithelia perfectly intact. As soon as the inflammation enters the subacute or chronic stage, their character changes and fat-globules appear. We can then no longer consider them pure epithelial casts.

3. *Blood Casts* (see Fig. 67).—The presence of blood casts in the urine always shows a hemorrhage within the tubules of the kidney, and, when seen in large numbers, the complication is quite grave; but less so in children than in adults. The appearance of these casts varies greatly; they are usually more irregular than the epithelial casts, their ends more or less rounded, and they may be either studded with a varying number of red blood-corpuscles without changing their color, or, if they have been retained in the tubules for some time, the blood-corpuscles lose their shape, and the casts take on the appearance of dark, rust-brown, granular clusters.

Many of these casts may show transitional forms and are more or less distinctly colored. They always indicate an acute hemorrhagic process, and usually we find either hyaline or epithelial casts, or both, with them. Besides these, conglomerations of fibrin, the so-called fibrin casts, are occasionally found, but, properly speaking, they are not true casts. In the rare cases of hæmoglobinuria, irregular, dark casts, which appear granular and are composed of disintegrated blood corpuscles—the so-called hæmoglobin casts—may be quite abundant.

4. *Granular Casts* (see Fig. 68).—While the three varieties of casts just described are always found in acute cases or fresh acute exacerbations

of chronic inflammations, granular casts rarely appear in strictly acute inflammations. As a rule, they are not formed until a number of weeks after the beginning of the disease; but in some cases, especially in children in whom a nephritis develops after contagious diseases, such as scar-

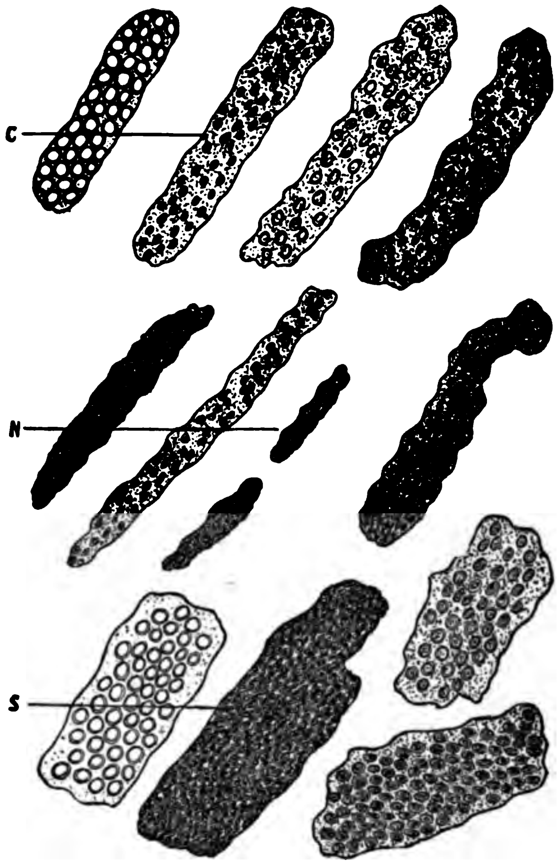

FIG. 67.—BLOOD CASTS (× 500).
C, Casts from convoluted tubules; *N*, from narrow tubules; *S*, from straight collecting tubules.

let fever and diphtheria, they may be seen in small numbers one or two weeks after the first symptoms of the nephritis have set in.

Granular casts are either perfectly regular and have sharply defined contours, or they are more or less curved, or appear curved at one side while they are straight at the other. Their ends are either rounded or partly broken, and they may be broader at one place and narrower in another—a peculiarity especially pronounced in those from the narrow tubules. Their degree of refraction changes considerably, and they sometimes appear yellowish, at other times colorless.

The granulation of these casts varies to a great degree, some being coarsely granular, others finely granular, still others partly the former and partly the latter. They may appear coarsely granular at both ends,

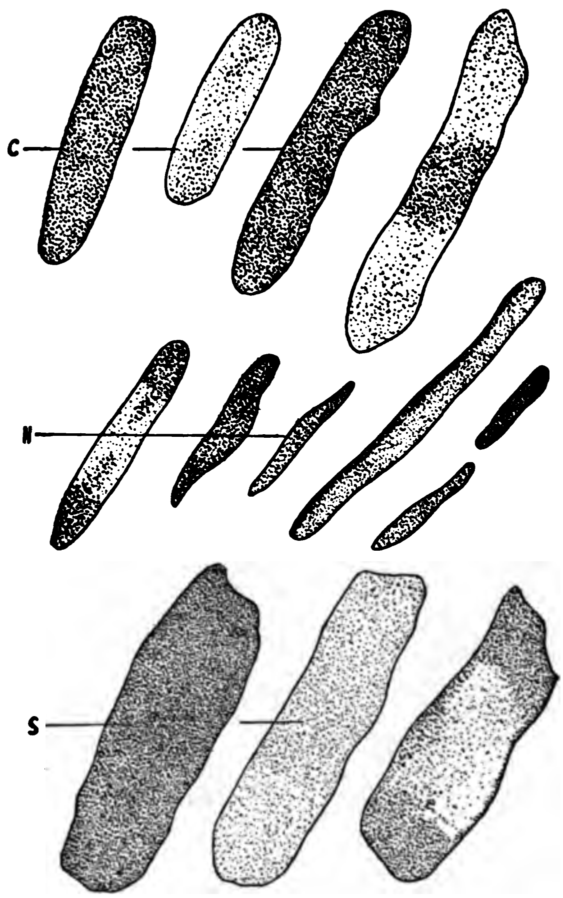

FIG. 68.—GRANULAR CASTS (× 500).
C, Casts from convoluted tubules; *N*, from narrow tubules; *S*, from straight collecting tubules.

finely granular in the centre, or finely granular above and below and coarsely granular in the centre, the gradations being many.

Granular casts are probably due in most cases to a disintegration of the kidney epithelia, which will commence after a varying length of time. In those cases which have not as yet become chronic, the disintegration of the epithelia can be studied under the microscope in all the different stages. In cases of long duration the granules become changed into glistening fat-granules and -globules.

5. *Fatty Casts* (see Fig. 69).—True fatty casts are always secondary products of epithelial and granular casts, therefore their size and shape

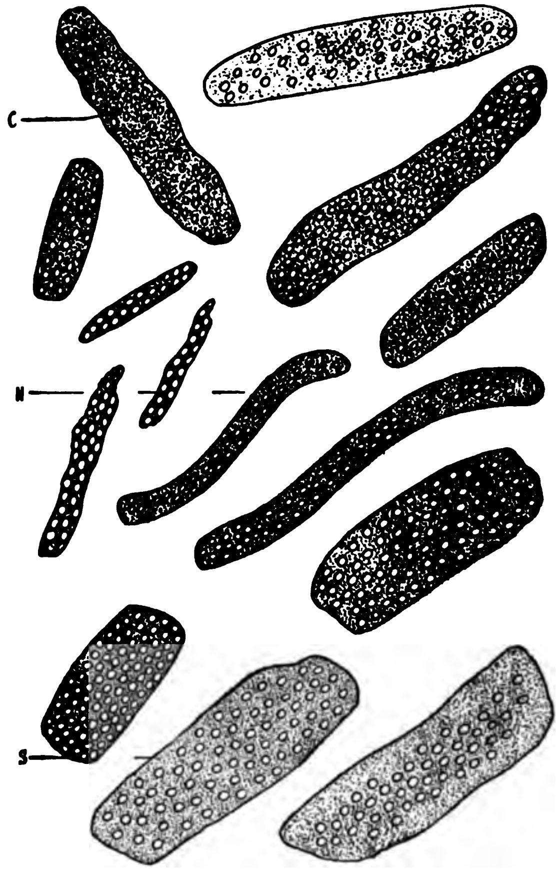

FIG. 69.—FATTY CASTS (× 500).
C, Casts from convoluted tubules; *N*, from narrow tubules; *S*, from straight collecting tubules.

resemble the former considerably. The substance of all the casts so far mentioned is the same, the difference in appearance being given by the outer adhering formations. Conglomerations of variously sized, sometimes large, fatty globules, without well-marked contours, showing their original substance, cannot be classed as true casts.

Fatty casts contain a varying number of small, glistening fat-globules and -granules, which give to the cast a high refraction, the cast being either completely or partially filled with them. As they are secondary products only, it follows that, even when they are present in small numbers, the diagnosis of a chronic process is justified; the more so, the more completely they are formed. The commencement of their formation can

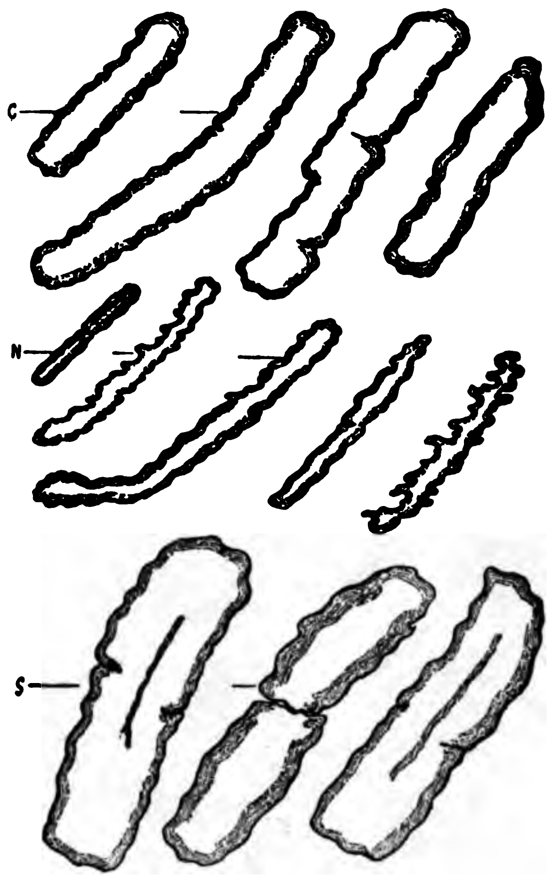

FIG. 70.—WAXY CASTS (× 500).
C, Casts from convoluted tubules; *N*, from narrow tubules; *S*, from straight collecting tubules.

frequently be seen in both epithelial and granular casts, the granules becoming more glistening and highly refractive, and finally changing to globules. When the casts are present in large numbers, they always denote a pronounced fatty degeneration of the kidney, as found in the large white kidney.

6. *Waxy Casts* (see Fig. 70).—Waxy casts are different in their chem-

ical nature from hyaline casts; they are characterized by wavy, fluted contours, a high refracting power, a more or less yellowish color, and a high degree of brittleness. They vary greatly in size, and are always more or less irregular, on account of their frequently broken contours. Sometimes their wavy, fluted appearance is extremely pronounced, and they may resemble regular corkscrew windings.

FIG. 71.—MIXED CASTS (× 500).

When all these characteristics are present the diagnosis of a waxy cast is plain, and such a cast never appears in acute inflammations, but only in chronic processes, which, if the casts are at all numerous, are always intense. They invariably signify waxy degeneration of the kidney. Sometimes hyaline casts exhibit spiral windings, and may somewhat resemble waxy casts. These spiral windings are probably due to their having originated in the spiral portion of the ascending branch of the loop tubule, and have no special significance. Such hyaline casts are never of the same high refraction as the waxy casts, and a little care is sufficient to differentiate them from each other.

Pure waxy casts may be found studded with different formations, which, of course, does not change the character of the cast. At times they are of extremely large size, and may then be almost entirely broken in different portions.

7. *Mixed Casts* (see Fig. 71).—In a large number of cases, when casts are present, these casts do not appear in their true form, but may be more or less mixed. Any two, three, or four varieties may be so intermingled as to be difficult of differentiation. The more common of these forms will be found in Fig. 71.

In the first row, the first cast shows an epithelial-granular-fatty variety, with the epithelia perfectly intact; while the other casts partly show how the epithelia break down and become disintegrated into granules and fat-granules and -globules, partly the change of granular into fatty casts. The disintegration of the epithelia, in the manner here depicted, is frequently seen in subacute inflammations. The change of granular casts into the fatty kind is seen in chronic processes.

In the second row, combinations of waxy casts are shown, the first being a fatty-waxy; the second, a granular-fatty-waxy; while the third and fourth are blood-waxy casts. The first cast in the third row is an epithelial-blood cast; the second, a blood-epithelial-granular-fatty cast; and the third, an epithelial-granular-fatty-waxy cast. The diagnosis of a case does not, of course, become altered by these combinations.

Other Casts.—Besides these six varieties of casts, the mucus-casts or cylindroids, previously described, are occasionally placed among the true casts; that they do not have any special significance has already been stated. They may contain a varying number of fat-globules, but their striated, irregular appearance is sufficient to clear up the diagnosis.

Again, a separate variety of casts is described as being derived from the seminal tubules. These casts are said to resemble hyaline casts, but to differ from them in their larger size, greater breadth, and greater irregularity. They are, however, nothing but cylindroids, and, as such, have no special significance.

II. *FALSE OR PSEUDO-CASTS.*

False or pseudo-casts are not infrequently found in the urine, and have no connection whatever with diseases of the kidney. These formations are mostly conglomerations of different substances upon mucus-threads or -casts, or accidental formations in the shape of casts. When true casts, especially of the hyaline variety, are present, together with an abundance of urates, the latter may undoubtedly be found upon the casts to such a degree as to render a diagnosis of the original cast doubtful.

Urate Casts (see Fig. 72).—Among these formations, conglomerations of urates, sometimes called uric-acid casts—although uric acid, as such,

FIG. 72.—CASTS OF AMMONIUM URATE AND SODIUM URATE (× 500).

rarely enters into their structure—as well as casts of sodium urate, are not infrequently found. The former, consisting of conglomerations of ammonium urate, are described as occurring only in infants, and forming in them small, reddish-brown masses, apparent to the naked eye: but they are also seen in adults, although very rarely. Formations of sodium urate, resembling casts, may at times be mistaken for granular casts; but they have the characteristic yellowish-brown color of sodium urate, and show no outlines in many cases. When the masses of sodium urate are not heavy, mucus-threads or -strings can be distinctly seen underlying them. Besides these, we may also see such formations composed of granules of sodium urate changing to globules and dumb-bells. When the

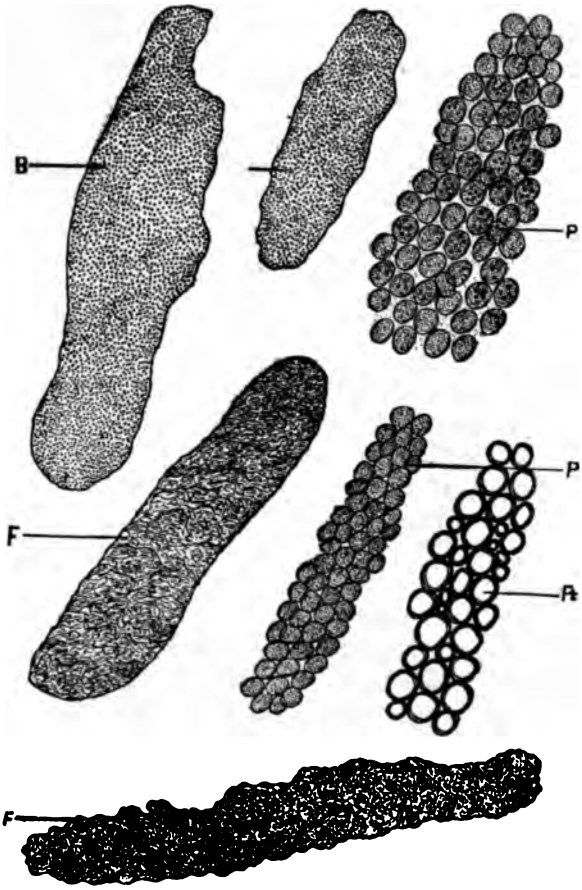

FIG. 73.—FALSE OR PSEUDO-CASTS (× 500).
B, Bacterial casts; *P*, pus casts; *Ft*, fat cast; *F*, fibrin casts.

change has advanced to a considerable degree, some of these formations may resemble disintegrated blood- or hæmoglobin casts, and great care must be taken not to mistake such urate casts for blood casts. Here, too, the absence of a contour, as well as the color of the urates, will be sufficient for a diagnosis.

Among the other pseudo-casts, the more common are bacterial, pus, fat, and fibrin casts (see Fig. 73).

Bacterial Casts.—Bacterial casts are of frequent occurrence, especially when the urine has been allowed to stand in a warm room for twelve hours or more, so that a large number of bacteria have developed. They undoubtedly resemble granular casts so much as sometimes to require a sharp focusing for their differentiation. They may vary considerably in size, but their outlines are pale and more or less irregular, and they are composed of masses of micrococci, not of granules. They have no significance whatever, except when found in perfectly fresh urine as an aid to diagnosis, where they are most likely to be seen in severe inflammatory or suppurative processes. As a rule, the micrococci become deposited upon mucus-threads. In order to clear up their diagnosis, it may, in rare cases, be necessary to add a drop or two of some strong mineral acid or alkali, to which they will be seen to have a great resistance.

Pus Casts.—Pus casts—that is, cast-like conglomerations of pus-corpuscles, usually upon mucus—are found in some cases. The pus-corpuscles may be massed together, with no outlines visible, or they are more loosely arranged, and may contain a number of small fat-globules. Pus-corpuscles may, of course, be found in small numbers upon different true casts, such as hyaline or epithelial, but such formations cannot be classed as pus casts.

Fat Casts.—Pseudo-fat casts are rare, but have been found in a few cases of so-called lipuria. They consist of large fat-globules, of a very high refraction, and occasionally containing margaric-acid needles. Again, a number of extraneous fat-globules upon mucus-threads have been seen; but these have a yellowish color, and can easily be differentiated.

Fibrin Casts.—Lastly, fibrin casts may be found in cases of hemorrhage. They may be of large size, have irregular, more or less sharply defined contours, and are of a yellowish or yellowish-brown color. They consist of small, wavy, irregular fibres, and never occur without the presence of characteristic strings or bands of fibrin. In cases of hemorrhagic parenchymatous nephritis, true blood casts are always associated with them.

Besides hæmoglobin, which may occur in the form of casts, two other varieties of pseudo-casts have been described, namely, pigment and cholesterin casts. Peyer has seen one specimen of each of these, but they are the rarest formations in urine.

CHAPTER XIV.

MICRO-ORGANISMS AND ANIMAL PARASITES.

I. *MICRO-ORGANISMS, OR FUNGI.*

PERFECTLY fresh urine normally does not contain any micro-organisms and can be considered sterile when obtained directly from the bladder; it may, however, be contaminated, when voided, by bacteria present in the urethra and especially the vagina. When allowed to stand, bacteria usually develop in a short time, even in originally sterile urine. In pathological conditions, on the other hand, bacteria may be present in large numbers when voided; such urine is always more or less turbid, and here the designation *bacteriuria* can be used.

The development of bacteria in urine may be slow or rapid, depending partly upon the reaction and partly upon the temperature. In an alkaline urine they develop rapidly, and in a warm temperature are usually found in large numbers one or two hours after the urine is voided. Bacteria present when the urine is passed may be derived from any portion of the genito-urinary tract or may be transported through the blood stream.

Micro-organisms seen in urine are divided into non-pathogenic and pathogenic. The former may belong to either the class of mould fungi, to that of yeast fungi, or to that of fission fungi; while the latter belong to the class of fission fungi.

Non-pathogenic Micro-organisms. 1. *Mould Fungi.*—Mould fungi, or *hyphomycetes*, found in urine are either *oidium*, *penicillium glaucum*, or one of the *aspergilli*, the latter being comparatively rare. These fungi will be seen only in acid urine, or urine which was originally acid, even though it has become alkaline.

The most common of the hyphomycetes is the *oidium lactis*, composed of conidia and mycelia (see Fig. 74). It easily develops in small numbers in urine of a highly acid reaction, and can be seen with the naked eye, in the form of whitish masses, only when present in large amount. Such urines contain a varying number of small globules, in which frequently a central so-called vacuole is observed, together with threads of mycelia, either narrow and short, or quite large and branching. The globules are the spores or conidia, and care must be taken not to mistake them for red blood-corpuscles or even fat-globules, which they may resemble. They vary in size, and can generally be distinguished by the central vacuole. The threads are the mycelia, which are, as a rule, coarsely granular and segmented, and contain a number of spores. They

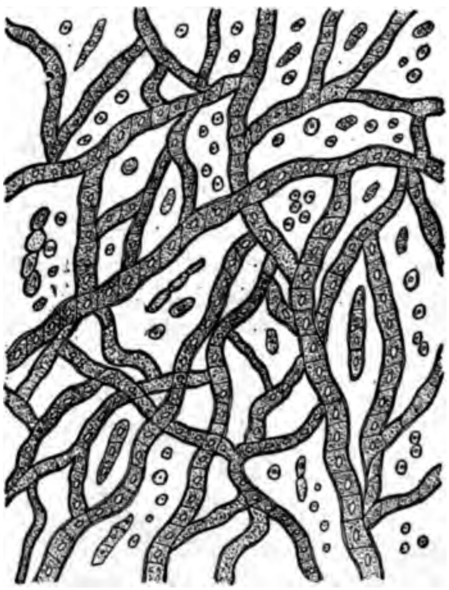

FIG. 74.—OIDIUM LACTIS (× 500).

may be mistaken for mucus, connective tissue, or even granular casts from the narrow tubules, from all of which they differ, however, by their peculiar, rather high refraction.

Besides the oidium lactis, both the *penicillium glaucum* and different varieties of *aspergilli* may be found in the urine, the former being quite common (see Fig. 75). The diagnosis of penicillium or aspergillus can be made only by the characteristic fruit-bearer or sporangium arising from the hypha. In penicillium glaucum, the most common mould fungus, the hyphæ divide and subdivide into thread-like formations—the basidia and sterigmata—the ends of which latter are surmounted by a number of spores or conidia. In the aspergilli no division takes place, but the hypha terminates in a spherical or club-shaped vesicle, from the periphery of which a number of short flask-like formations—the sterigmata—are visible, each of which contains a single spore upon its upper end.

2. *Yeast Fungi* (see Fig. 76).—The yeast fungi, or *saccharomycetes*, are found in acid urine, and are most frequently seen in those containing sugar, where they may be present in large numbers. They consist of va-

riously sized globules or cells, the larger of which contain a smaller globule or nucleus. They never form mycelia, but multiply by sprouting or budding. The globules have an oval or round shape, lie either singly, in twos, or in groups of different sizes, and are frequently beaded. In the

FIG. 75.—PENICILLIUM GLAUCUM AND ASPERGILLI (× 500).
The upper half of the drawing shows the penicillium glaucum, the lower half different varieties of aspergilli found in urine.

larger globules the process of budding can be plainly seen. The smaller globule, or daughter-cell, sprouts out from the larger or mother-cell, becomes an independent formation, grows, and, in its turn, forms a mother-cell. These globules may undoubtedly resemble blood-corpuscles, but their irregular size and shape, together with the presence of the nucleus, will be sufficient to differentiate them.

3. *Fission Fungi* (see Fig. 77).—The fission fungi, or *schizomycetes*, are rarely seen in highly acid urine, but frequently in urine which is becoming alkaline or has already undergone an alkaline change and is showing

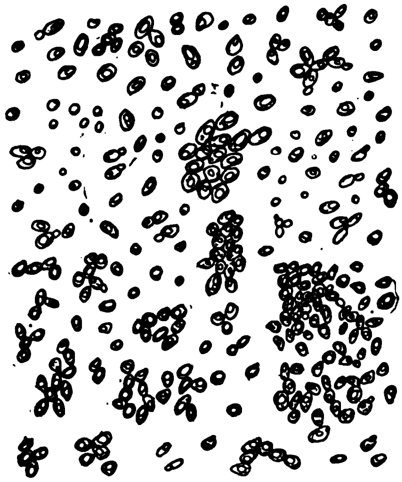

FIG. 76.—SACCHAROMYCETES (× 500).

putrefaction. When they are present in large numbers the urine is always cloudy, and both cocci and bacilli may be found. Of the former, the most numerous are large cocci, lying either irregularly or in small chain form—the *micrococcus ureæ*. This coccus, to a great degree, causes ammoniacal decomposition of the urine, the urea being transformed by it into ammonium carbonate. In urines containing pus-corpuscles in large numbers, both *staphylococci* and *streptococci pyogenes*—the former being small cocci grouped in variously sized, irregular bunches, and the latter in longer or shorter chains—will also be seen. Besides these, the so-called *zoöglœa* groups of cocci—cocci arranged in more or less regular masses—enveloped in a colorless, gelatinous capsule, may also be found, as well as large cocci, the *sarcinæ urinæ*, which are united into packets resembling corded bales of cotton, and are usually smaller than the sarcinæ found in sputa. Staphylococci and streptococci pyogenes are pathogenic, and may be found in any inflammatory condition.

Bacilli are usually present in varying numbers with the cocci, and are of different sizes, some of the small ones occasionally lying in twos, being formerly called *bacterium termo*, one of the varieties of putrefactive bacilli which cause ammoniacal decomposition of urine. Others, among them the *bacillus* or *bacterium ureæ*, are larger, and there are still others larger than the latter, among which the *bacillus subtilis*, or hay bacillus, is common. These bacilli are found to have a varying amount of motion, some being very active, others only slightly movable, and some without motion.

Besides the single bacilli, the urine not infrequently contains threads, composed of individual rods—the leptothrix threads—which may be quite abundant. There are cases of chronic cystitis, in which the urine, when voided, contains leptothrix threads in large numbers, and in which the cystitis seems to be caused by the leptothrix; these threads may lie upon as well as between the epithelia. In such cases whitish masses of small size are found in the freshly voided, cloudy urine, and when examined under the microscope are seen to consist of conglomerations of bladder epithelia with many leptothrix threads. Cases of this kind may last for many years, and frequently recur in spite of all local treatment.

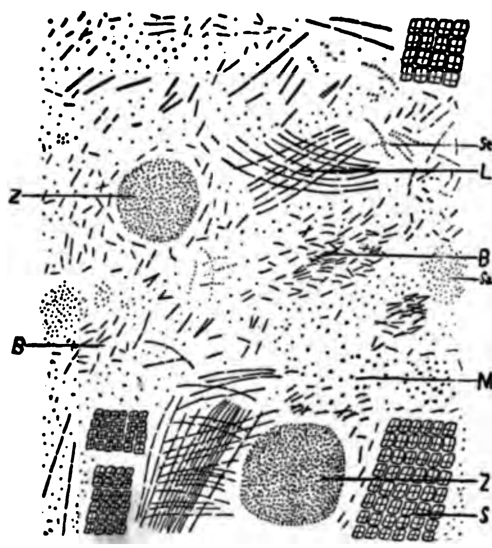

FIG. 77.—SCHIZOMYCETES (× 500).
B, Bacilli; *St*, streptococci; *Sa*, staphylococci; *L*, leptothrix; *MU*, Micrococcus ureæ; *Z*, zoöglœa; *S*, sarcinæ.

Pathogenic Schizomycetes.—Among the pathogenic bacteria, the most important are undoubtedly the *gonococci* and *tubercle bacilli*, which are not infrequently found in urine, and for which careful search must, when necessary, be made. For the detection of these, it will always be necessary to color the specimens, and the mode of procedure is the following: Select the thickest portion of the urinary sediment, best obtained by the use of the centrifuge, or the filaments, if any are present, as will be the case in chronic gonorrhœa, and by means of a sterilized needle spread carefully over perfectly clean cover glasses, taking never less than two, but preferably three or more. Allow the glasses to dry thoroughly, and draw them through the flame of an alcohol lamp or a Bunsen burner in a moderately quick manner, specimen side upward, three times, partly to fix the specimen upon the cover glass, and partly to coagulate the albuminous substances present. Then color the specimen with an aniline color, either fuchsin, methylene blue, or gentian violet.

Gonococci.—In searching for gonoccoci in the urine, the cover glasses are best colored, for a few seconds to one or two minutes, either with a plain watery fuchsin solution, made by taking one part of a concentrated alcoholic fuchsin solution (one part of fuchsin in substance to four or five of absolute alcohol) to eight, ten, or twelve parts of distilled water; or with a methylene-blue solution—fifty to sixty drops of a concentrated alcoholic solution (one part of methylene blue to four or five of absolute alcohol) to one ounce of water. Methylene-blue solution may also be made by taking 30 c.c. of a concentrated alcoholic methylene-blue solution and 100 c.c. of 0.01 per cent caustic potash; this is Loeffler's alkaline methylene-blue solution. Any one of these solutions, if carefully made, will keep a long time, and is always ready for use.

After having passed the cover glasses through the flame, as just described, a small amount of the coloring solution is dropped upon the specimen and allowed to remain for from a few seconds to a minute or two, the former being sufficient when fuchsin is used, the latter being necessary when methylene blue is employed. After coloring, the cover glass is rinsed in water, the lower surface dried, and the specimen either at once mounted upon a slide and examined in water or dried and mounted in a drop of Canada balsam.

In searching for gonococci, it is always best to use an immersion lense and a magnifying power of 900 or 1,000 diameters, although a power of 700 or 800 diameters is sufficient. In specimens so prepared, the gonococci, as well as the nuclei of the pus-corpuscles and epithelia, are colored. The pus-corpuscles contain one or more nuclei.

In cases of acute gonorrhœa (see Fig. 78) the gonococci, or *micrococci gonorrhœæ*, are found in large numbers in the urine, not as numerous as in the gonorrhœal pus taken directly from the orifice of the urethra, but still very abundant. They are seen both in the pus-corpuscles and lying free in variously sized groups. The pus-corpuscles are numerous, and mucus-threads in small numbers are always present. Urethral epithelia are also usually found, and may contain groups of gonococci.

Gonococci were first discovered by Neisser in the year 1879, and cultivated by Bumm in 1885. They are, as a rule, found in twos, either singly or in groups, with the adjacent surfaces flattened and separated by a colorless interspace, giving the so-called biscuit shape. The more or less regular groups of *diplococci* are found either entirely within the pus corpuscles or epithelia, or lying entirely free, but never half-way within and half-way free, though large groups, completely filling the pus-corpuscles, may slightly overlap the periphery. Again, no matter how completely the pus-corpuscles are filled with them, the nucleus or nuclei usually re-

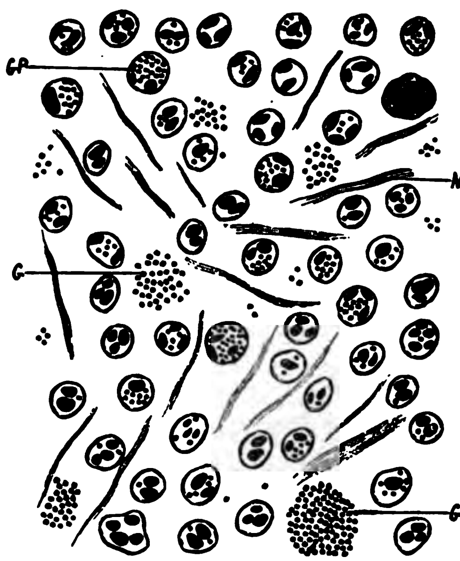

FIG. 78.—ACUTE GONORRHŒA (× 700).
G, Groups of gonococci; *GP*, pus-corpuscle containing gonococci; *MS*, mucus-thread.

main free, though here, again, individual cocci may be found upon the periphery of the nucleus. These features, though perhaps not absolutely characteristic, are sufficiently so for all practical purposes.

If any doubt remains about their character, Gram's method should be used. Color a few specimens with gentian violet, either a carbolic solution made by taking 10 parts of a saturated alcoholic solution of gentian violet and 90 parts of a five per cent watery carbolic acid, or an aniline solution, made by adding 5 parts of a concentrated alcoholic solution to 100 parts of aniline water (aniline oil 1 part, distilled water 20 parts, and filter) for a few minutes and subject to Gram's solution (pure iodine 1 part, iodide of potash 2 parts, and distilled water 300 parts) for one or two minutes. The specimens are now washed in alcohol, then rinsed in water and recolored with a one or two per cent aqueous solution of Bismarck brown for one-half to one minute, again rinsed in water, dried and examined. Gonococci are Gram-negative.

When subjected to this method, the gonococci have lost their original violet stain and have taken up the Bismarck brown, being, therefore, colored brown. This method at once differentiates them from the staphylococci, which retain their violet color. If all the features enumerated, especially their characteristic grouping within the pus-corpuscles, and the loss of their violet color by the last-named method, are present, no doubt whatever will exist as to the character of the cocci.

In acute cases of gonorrhœa the search for gonococci is very easy; but this becomes a more difficult matter in the chronic cases, where only a

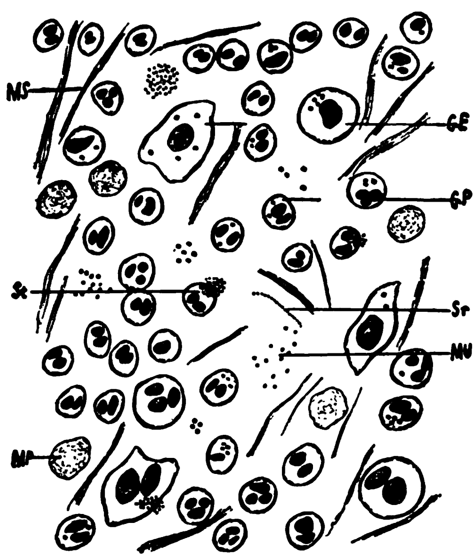

FIG. 79.—CHRONIC GONORRHŒA (× 700).

GP, Pus-corpuscles containing gonococci; *GE*, epithelium from the prostate gland containing gonococci; *St*, pus-corpuscles containing Staphylococci pyogenes; *Sr*, Streptococci pyogenes; *MU*, Micrococcus ureæ; *MS*, mucus-threads; *MP*, mucus-corpuscle.

small number of filaments may be found in the urine. Frequently it is of the utmost importance to determine the presence or absence of gonococci in such cases, and the filaments are subjected to the methods just described and carefully examined. As before said it is never advisable to depend upon a power of 500 diameters, but higher powers, preferably a homogeneous immersion lens, should be used, and a large number of specimens carefully examined. The features found in such a filament, containing gonococci, are shown in Fig. 79.

Pus-corpuscles are never so abundant in these cases as in the acute, and may even be quite scanty, but mucus-threads as well as corpuscles are numerous; epithelia from the urethra, and usually from the prostate gland, will also be seen. The gonococci are always found in smaller numbers, but only singly or in small groups, and the cocci seen should never be diagnosed as such unless some are found within the pus-corpuscles. Besides gonococci, such filaments always contain irregular groups of staphylococci; these may be either free or in groups, lying partly within pus-corpuscles and partly outside. In some cases streptococci, usually in rather small chains, are also present, as well as the micrococcus ureæ in chains or irregular small groups.

Occasionally it may be necessary to use culture media, although it is difficult to grow gonococci from urinary sediments. For this purpose either blood-serum agar or Loeffler's blood serum may be used, though some prefer media made with hydrocele or ascitic fluid and agar-agar. Even at best the growth of gonococci is slow and never very heavy.

Other Cocci.—Besides gonococci, other pyogenic cocci, both *staphylococci pyogenes* and *streptococci pyogenes*, are found in urine, but, as may be expected, only wherever there are large numbers of pus-corpuscles; they, therefore have little practical significance. The staphylococci are the *staphylococcus pyogenes aureus*, *albus*, and *citreus*, which can be differentiated only by culture methods. Besides the *streptococcus pyogenes*, a streptococcus, which cannot be distinguished from it, but has been described by Fehleisen as being the cause of erysipelas, may be found in all cases of erysipelas in which a nephritis is at the same time present. Micrococci have also been seen in the urine in septic processes, as well as in endocarditis.

Tubercle Bacilli.—The presence of *tubercle bacilli* in moderate numbers in the urine is always a symptom of tuberculosis somewhere in the genito-urinary tract. Its exact location can easily be determined by the characteristic epithelia. As a rule, they will be found in larger numbers only when a suppurative or an ulcerative process exists; and whenever the diagnosis of a suppuration or an ulceration can be made from the different features found in the urine, especially with all the evidences of a chronic condition, it will be best to examine for tubercle bacilli even though distinct clinical symptoms of a tubercular process have not as yet developed.

The search for tubercle bacilli in the urine is by no means an easy one; many drops may have to be examined before arriving at a definite conclusion. The appearance of the urine is no criterion, since bacilli may be present in small numbers in rather clear urine, though, as a rule, it will be more or less turbid. They can be found in either an acid, amphoteric or alkaline urine, but the presence of a large number of salts renders their detection still more difficult. In such cases it is advisable to dissolve the salts with a solution composed of 1 part of borax, 1 part of boric acid, and 25 parts of water, which is simply added to the sediment.

When a urine is to be examined for tubercle bacilli it should be fresh and, preferably, it should be obtained by catheter after thoroughly cleansing the external genital organs, to prevent the admixture as much as possible of putrefactive microorganisms, and especially of the smegma bacillus. The latter, like the tubercle bacillus, is an acid-fast microorganism, resembling the tubercle bacillus to a considerable degree, and is not infrequently present on the external genitals of both sexes. The fresh urine, which should, if possible, be placed in a sterile bottle, is now allowed to stand in a cold place for six hours, so that a sediment forms by gravity; the supernatant fluid is then carefully decanted, the sediment put in the centrifuge tubes and centrifugalized for three minutes. Of the sediment obtained in this manner, the thickest portion is selected and a number of smears made upon perfectly clean slides or cover glasses. After they are perfectly dry, they are fixed by passing them through the flame of a Bunsen burner or an alcohol lamp three times, specimen side upward. Specimens obtained in this manner by double sedimentation, that is gravity and the centrifuge, give better results than when the urine is centrifugalized at once.

Ellerman and Erlandsen* allow the catheterized urine to settle, decant the supernatant fluid, centrifugalize, mix the sediment thus obtained with four times its bulk of a 0.25 per cent solution of sodium carbonate, and place it in the incubator for twenty-four hours at 37° C. (98½° F.). If the reaction is still acid, they add a little more sodium carbonate and allow the digestion to continue somewhat longer. They now decant the upper layer of the supernatant fluid and centrifugalize the remainder. To the sediment left then, after pouring off the upper fluid, they add four times its volume of a 0.25 per cent solution of sodium hydroxide and stir with a glass rod till dissolved. The whole is then heated to boiling over the water bath; after cooling it is once more centrifugalized, and the sediment thus obtained is used for staining. This somewhat complicated method is, as a rule, unnecessary, but in those cases in which the clinical symptoms point to a tubercular process in the genito-urinary tract, and tubercle bacilli can not be found by the simple methods of sedimentation, it possesses its advantages. Small numbers of tubercle bacilli can not infrequently be found by this method, after other means have failed.

The staining methods employed for detecting tubercle bacilli are

* Journ. of Am. Med. Assoc., Sept. 19, 1908.

numerous, but the simplest and best is the Ziehl-Neelsen carbol-fuchsin method. The staining solutions necessary are, first, a carbolic acid fuchsin solution, prepared by dissolving 1 gm. of fuchsin* in 10 c.c. of absolute alcohol and adding 90 c.c. of a five per cent aqueous carbolic acid solution; and second, Loeffler's methylene blue solution, made by taking 30 c.c. of a saturated alcoholic solution of methylene blue and 100 c.c. of a 0.01 per cent aqueous solution of caustic potash. The dried and fixed smear is covered with the carbol-fuchsin and heated, until it steams, over an alcohol flame or a Bunsen burner; the warm specimen is then set aside for from five to ten minutes, at the end of which time the tubercle bacilli are stained. It is not a good plan to boil the solution upon the smear over the flame for one or two minutes, as was formerly advised, since the specimen decolorizes less rapidly than by simple steaming. If a number of specimens are to be stained at once, it is best to make cover glass smears, float these in a watch glass filled with the fuchsin solution, specimen side down, heat for a few minutes to steaming, but not to boiling, and leave the specimens in the warm solution for a few minutes longer. Instead of warming the solution, a cold solution may be used, but then it is necessary to stain the specimens for about two hours instead of five to ten minutes.

Aniline-fuchsin may be used instead of carbol-fuchsin; this is made by adding enough of a concentrated alcoholic fuchsin solution (1 part of fuchsin to 5 parts of absolute alcohol) to aniline water (1 part of aniline oil to 20 parts of distilled water and filter) until saturation takes place; that is, until a distinct film appears at the top of the solution; this is usually one part of the alcoholic solution to eight or ten of aniline water. This solution, however, does not keep well and staining with it is slower, though the method, originally employed by Koch, is an excellent one; about twenty minutes are required for staining with the warm solution.

After the specimens are stained they must be decolorized. The tubercle bacilli stain slowly, but are then not readily decolorized, being both acid-fast and alcohol-fast, in contradistinction to most other bacteria, which will quickly lose their color when subjected to the action of acids and alcohol. Different acids may be used for decolorizing, but one of the best is a twenty to twenty-five per cent aqueous solution of nitric acid. The procedure is the following: After being stained, decolorize the smears with the nitric acid for a few seconds only, then thoroughly wash in a sixty per cent solution of alcohol until all color has disappeared, place specimen in absolute alcohol for a few minutes, wash in water, and at once recolor for about one-half minute with methylene blue, again wash in water, dry and specimen is ready for

* Acid fuchsin must not be used for tubercle staining.

examination. If cover glasses have been used for making the smear, mount upon a slide with a drop of Canada balsam. Instead of nitric acid a ten per cent solution of sulphuric acid in alcohol may be used, and the decolorizing agent allowed to act until the specimen is practically decolorized, when it is washed in water and restained; or a two or three per cent alcoholic solution of hydrochloric acid may be used. Gabbett's method of using a sulphuric acid-methylene blue solution (methylene blue powder 1 or 2 parts, 25 per cent sulphuric acid 100 parts) thus decolorizing and counter staining at the same time, is not advisable in urine work.

In specimens prepared in this manner, the tubercle bacilli, if any are present, are seen as bright red rods of varying lengths, either single, in

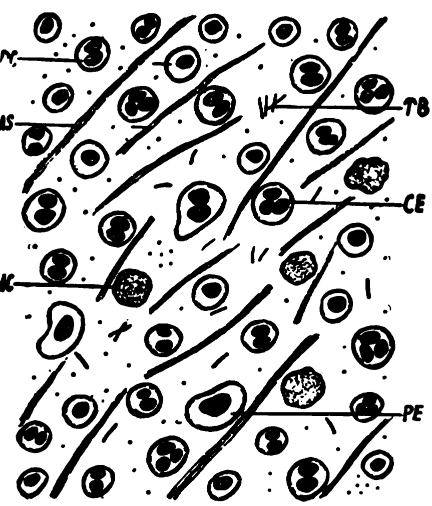

FIG. 80.—TUBERCULOSIS OF THE KIDNEY (× 650).

TB, Tubercle bacilli; *PC*, pus-corpuscle; *CE*, epithelium from convoluted tubules of kidney; *PE*, epithelium from pelvis of kidney; *MS*, mucus-threads; *MC*, mucus-corpuscle.

twos forming acute angles or crossed, or in groups, partly straight, partly bent or curved and occasionally showing branching forms; not infrequently they appear beaded, giving the appearance of a number of cocci joined together. Their number in urine varies greatly; sometimes they are so scanty that two or three specimens have to be examined before any are found, at other times they are so numerous that every field contains them, and they may be seen in clumps containing ten, twenty, thirty, or considerably more, bacilli. All the other features are colored blue.

A specimen of tuberculosis of the kidney, colored in this manner, is shown in Fig. 80. The features which can easily be recognized are tubercle bacilli in moderate numbers, pus-corpuscles, epithelia from the convoluted tubules of the kidney, epithelia from the pelvis of the kidney, mucus-threads, mucus-corpuscles, and various cocci.

Care must be taken not to mistake the harmless smegma bacillus, which is frequently present in the urine, resembles the tubercle bacillus, and is also resistant toward acids, for the tubercle bacillus. The smegma bacillus, however, does not resist absolute alcohol for any length of time, so that, when its presence cannot be excluded, it is best to subject the specimen for ten to twenty minutes to alcohol after being treated with the acid. The tubercle bacillus is not affected by the alcohol.

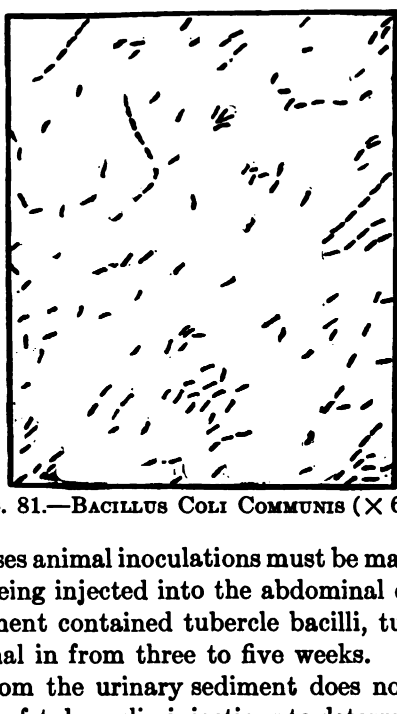

FIG. 81.—BACILLUS COLI COMMUNIS (× 600).

In doubtful cases animal inoculations must be made, a small amount of the sediment being injected into the abdominal cavity of a guinea-pig. If the sediment contained tubercle bacilli, tuberculosis will develop in the animal in from three to five weeks. The cultivation of tubercle bacilli from the urinary sediment does not give satisfactory results. The use of tuberculin injections to determine the presence or absence of tuberculosis is also recommended.

Typhoid Bacilli.—Among the other pathogenic bacilli found in urine, the *typhoid bacilli* have been discovered in large numbers in cases of typhoid fever, though never at the commencement of the disease, and they are not, therefore, of much practical value for the diagnosis. Poniklo, in the year 1892, was the first to call attention to the presence of typhoid bacilli in the urine, and since then the bacilli have been found by different observers. In most cases described, the evidences of a more or less pronounced nephritis or of a hemorrhage were also present. The bacilli may persist in the urine for weeks and even months, and may be extremely abundant.

Bacillus Coli Communis.—The *bacillus coli communis* (see Fig. 81) is not infrequently present in urine, especially in pronounced inflammations, such as nephritis, pyelitis, and cystitis; it may be found in large numbers, and seems to be a rather common cause of cystitis. This bacterium is a short, thick rod, found also in twos, small chains, and groups. It has a moderately active motion. In the year 1895 Pluym and Laag described it as the sole cause of a urethritis which gave all the symptoms of a gonorrhœal infection, in which gonococci were entirely

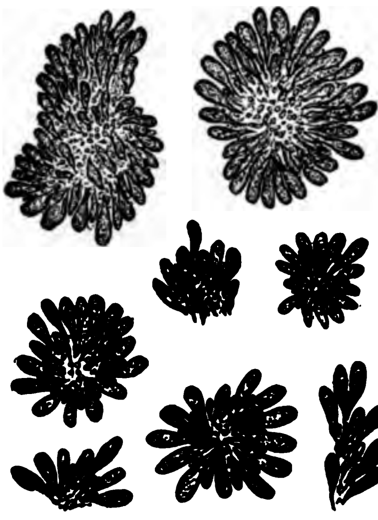

FIG. 82.—ACTINOMYCES (× 500).

absent, but the bacillus coli communis was found in large numbers, lying mostly within the pus-corpuscles and epithelia.

Other bacilli have also been described as being present in various diseases of the genito-urinary tract, but they are of no diagnostic value.

Actinomyces.—The fungus known as *actinomyces* (see Fig. 82) is of rare occurrence in the urine, but is undoubtedly found in actinomycosis of the internal organs, where the disease affects the genito-urinary tract. Its classification is still undecided, but it seems to stand in an intermediate position between the bacteria and the higher fungi.

The fungus consists of variously sized conglomerations of highly refractive, irregular, club-shaped masses. The club-shaped, cylindrical, or pear-shaped masses terminate toward the centre in a point or fibrilla, which loses itself in a mass of granules, amid other similar fibrillæ. The individual club-shaped elements greatly vary in length, but all terminate in the centre.

The urine from which the accompanying drawing was made was turbid when passed and gave all the macroscopical evidences of a chronic cystitis. It contained a few small granular masses which proved to be actinomyces. The features present under the microscope were numerous, and conclusively showed a chronic ulcerative process in the bladder. There were pus-corpuscles in large numbers; epithelia from the bladder, especially cuboidal and columnar; numerous connective-tissue shreds; fat-granules and -globules; large zoöglœa masses; mucus-threads and -corpuscles, and the actinomyces fungus, which was perfectly characteristic, so that the diagnosis of a chronic ulceration of the bladder, due to actinomyces, could easily be made. The reaction of the urine was alkaline.

II. *ANIMAL PARASITES, OR ENTOZOA.*

Trichomonas Vaginalis (see Fig. 83).—Of all the animal parasites, the most common is the *trichomonas vaginalis*, which belongs to the class of flagellata. It occurs in the urine of females, being a frequent but per-

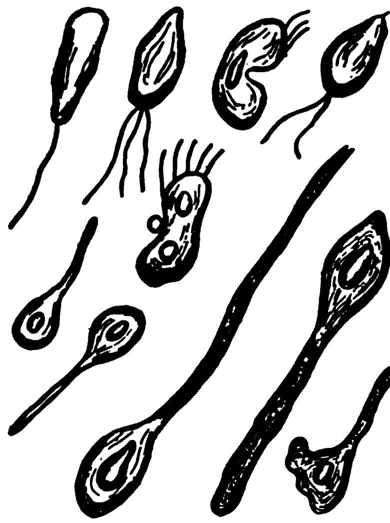

FIG. 83.—TRICHOMONAS VAGINALIS (× 500).

fectly harmless inhabitant of the mucosa of the vagina in cases of leucorrhœa. Although it has no pathological significance, its occurrence and shapes must be known, since it otherwise might be mistaken for different formations, especially when small.

Trichomonas is of an oval or somewhat irregular form, and usually has a tail-like extremity. This extremity, mostly of the same size as the body or a little longer, may occasionally be three or four times that size, of con-

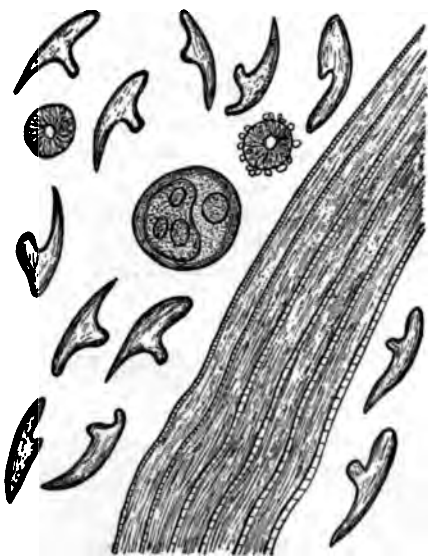

FIG. 84.—PORTIONS OF ECHINOCOCCUS (× 400).

siderable thickness, and striated. It may, however, be nothing but a small filament, like a flagellum. In the interior of the body one, two, or more small formations, similar to nuclei, may be seen. In many cases one or more cilia are given off from one extremity or side.

Echinococci (see Fig. 84).—These entozoa, although rare, do occasionally occur in the urine, and may either have developed directly from the urinary organs or have ruptured from some neighboring organ. The characteristic parts of the *echinococci* found in the urine are the hooklets as well as portions of the membrane; scolices may also be found.

The echinococci cysts, as such, will never be seen in the urine, and in a suspected case it may become quite difficult to find the characteristic portions. The scolices are small, usually round, and supplied with a wreath of hooklets. The individual hooklets do not vary in size to a great degree, and their shapes, although differing somewhat, are more or less identical. Parts of the membrane which have a concentric striation may at times be present. In the specimen from which the illustration was taken, the different portions here shown could be found only after patient search, but were characteristic.

In all cases in which parts of the echinococci are found in the urine, evidences of a hemorrhage or an ulceration, or both, will be present. As a rule, red blood-corpuscles are numerous, together with epithelia and

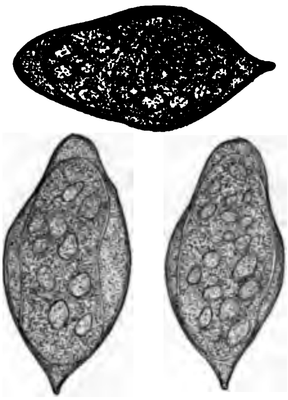

FIG. 85.—OVA OF DISTOMA HÆMATOBIUM (× 500).

connective-tissue shreds from the organ in which the cysts are located. Pus-corpuscles are usually abundant. When the echinococci have directly developed in the urinary organs, the kidney is the general location, and epithelia from both the convoluted and straight collecting tubules are present.

Distoma Hæmatobium (see Fig. 85).—The parasite *distoma hæmatobium*, or *Bilharzia hæmatobia*, so called from Bilharz, who first described it, has probably never been found in the urine, but its eggs do occur in some cases. It is common in tropical countries, especially in Egypt, and is found in the portal vein and its branches, the splenic and mesenteric veins, as well as in the venous plexuses of the rectum and bladder.

In our climate Bilharziasis is rarely found, but does occur. It may be seen in persons who have recently returned from the tropics, and the ova may be found in the urine in considerable numbers. The illustration was taken from such a case, and in every drop examined a dozen or more of the ova were present. They have an oval or flask-like shape, are large, and taper considerably at one extremity, the other being rounded. They consist of a moderately thick, highly refractive capsule, are coarsely granular, and contain quite a number of small, roundish, granular bodies within a membranous formation.

When these ova are found in the urine, blood-corpuscles, pus-corpuscles, and epithelia, usually from the bladder, are seen, showing a hemorrhage or inflammation of the bladder. In most cases fat-globules and -granules are also present in considerable numbers. The parasites may invade any portion of the urinary tract, especially the ureters and pelves.

Filaria Sanguinis Hominis (see Fig. 86).—This parasite is also of rare occurrence in our climate, but common in other climates, as in the West India Islands, Egypt, China, and Japan. It seems to be transferred to human beings through mosquito bites, and may be extremely abundant in the blood; in urine it may be found in varying numbers in such cases.

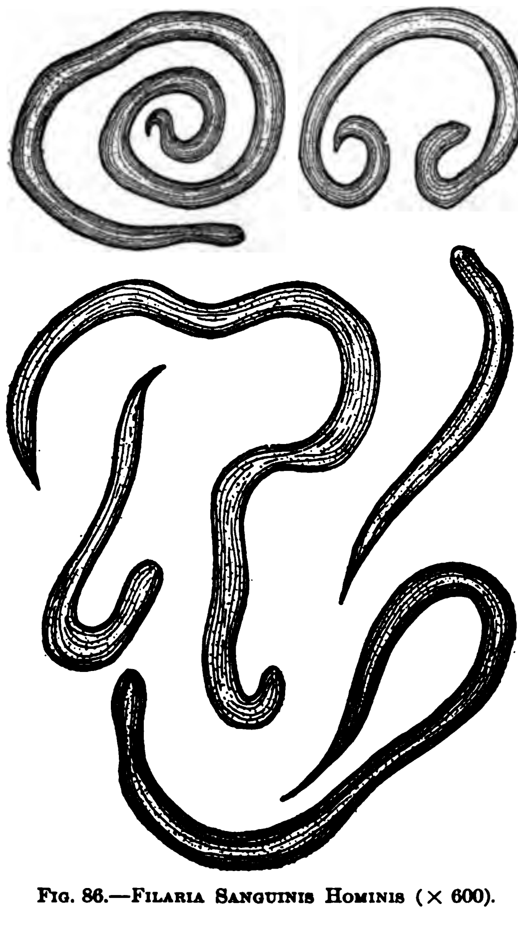

FIG. 86.—FILARIA SANGUINIS HOMINIS (× 600).

It consists of a cylindrically shaped body, a short, rounded head, and a long, thread-like, pointed tail. It is granular and frequently striated.

When the parasite appears in the urine, it may cause either severe hæmaturia or the condition known as chyluria, or more frequently both.

It is claimed that it may be present in perfectly clear urine, but this must be very rare, since, as a rule, the urine presents a milky appearance when voided, and upon examination is found to contain a large amount of fat, in the form of small globules and granules, as well as the evidence of a more or less pronounced hemorrhage. Pus-corpuscles, as well as different epithelia, are usually present in small numbers.

When such a milky urine, denoting chyluria, is examined, filaria must always be looked for, since the parasite is almost invariably the cause of this condition. It may be present in large numbers in the urine, so that there will be no difficulty in finding it; but, on the other hand, it may be scanty. In examining for filaria, it is advisable to take the first urine voided in the morning, since it is a well-known fact that the parasite is

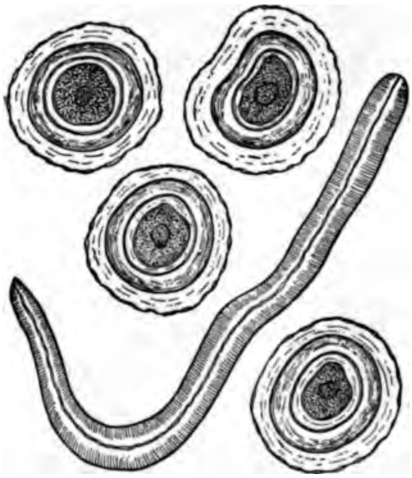

FIG. 87.—OVA AND PORTION OF ASCARIS LUMBRICOIDES (× 500).

active at night, or rather during the resting hours of the patient, and can then be found in large numbers in the blood, while it is quiescent during the working hours and cannot be found.

Ascaris Lumbricoides (see Fig. 87).—Although in rare instances only, the round worm, *ascaris lumbricoides*, of such common occurrence in the intestinal tract of children, may be found in the urine, having passed into the bladder through the urethra. Portions of the parasite and a number of ova will then be present in the urine.

The urine from which the illustration was taken gave all the features of a severe acute catarrhal cystitis. It contained a small number of minute particles, which proved to be the ova; also a part of the body of an ascaris. The ova, of a yellowish-brown color, are round formations, enclosed in a thin, irregular capsule and a somewhat thicker membrane;

the interior is coarsely granular and contains a nucleus. The parasite itself is of considerable size, has a cylindrical body, a narrower, tail-like extremity, and a head consisting of three papilliform nodules; it is found in the urine only in very rare instances.

Other Parasites.—Other parasites which may possibly be found in the urine are the *strongylus gigas*, *oxyuris vermicularis*, and the *cercomonas urinarius*. The strongylus gigas resembles the ascaris lumbricoides, although it is much larger, and its head contains six papilliform nodules instead of three. The oxyuris vermicularis is a small, thread-like formation, and the cercomonas urinarius a small flagellate, which consists of an oval, granular body, and contains a number of flagella. These parasites are rare and of little practical importance. The oxyuris vermicularis, the pin- or seat-worm, however, may migrate into the urethra, especially of females, exceptionally of males, causing a more or less pronounced irritation.

CHAPTER XV.

EXTRANEOUS MATTERS.

Extraneous matters are common occurrences in urinary sediments, and must be well known, as they might frequently lead to errors in diagnosis. Their presence in the sediment may be due to many causes, such as exposure to air, from which various objects may fall into the urine, pouring the urine into bottles which are not perfectly clean, the use of salves or dusting-powders for the genital organs, or admixture of particles

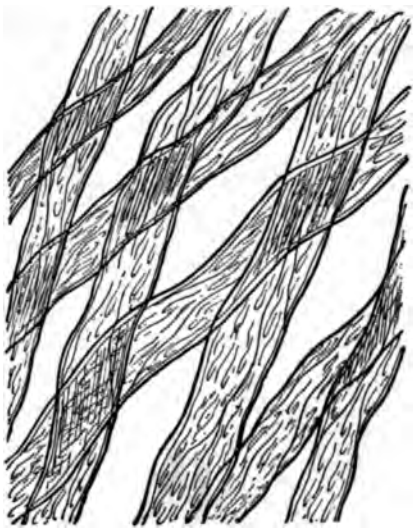

Fig. 88.—Cotton Fibres (× 500).

from the fæces. Many of these formations are characteristic enough, but others may closely resemble various features of normal or pathological urine, from which they must be carefully differentiated.

The different fibres of cotton, linen, silk, and wool are frequently found in the urine.

Cotton Fibres (see Fig. 88).—Cotton fibres are coarse, somewhat wavy and twisted. They are highly refractive, their edges being more compact than the centre. The central portion may appear slightly folded, and often shows irregular markings. When the fibres are very small, the diagnosis must be made from the wavy, compact appearance.

Linen Fibres (see Fig. 89).—Linen fibres are variously sized, sometimes broad, and at other times narrow. They are composed of smaller

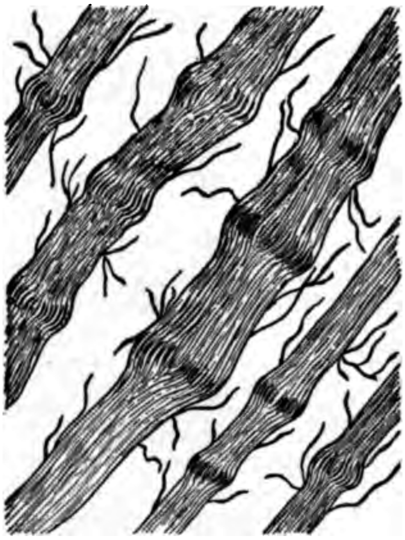

FIG. 89.—LINEN FIBRES (× 500).

fibrillæ, which, although quite refractive, are less so than cotton fibres. At different parts of the fibre, irregular transverse breaks are seen, which are caused by the process of hatchelling. The finest fibrillæ will be found broken off in a very irregular manner from the surface of the main fibre, being either long or short, and at times branching in different directions.

Silk Fibres (see Fig. 90).—Silk fibres are homogeneous, moderately shining; their cut ends are flattened by the blades of the scissors and rendered slightly jagged. If from woven goods, the fibres assume wavy or spiral impressions.

Wool Fibres (see Fig. 91).—Wool fibres are coarse, and have saw-teeth-like serrations along the edges, corresponding to the edge of the imbricated scales covering the cuticle; their structure is faintly striated. Hairs of different animals have different forms, and we may observe the central medullary canal and a varying amount of pigment.

Any of these fibres may be found dyed in different colors, which is sometimes quite misleading.

Human Hairs.—Human hairs are also not infrequently found in the urine, and may be known by the flat epidermal scales, firmly attached to each other, which form the main mass of the hair, and by the varying amount of pigment.

Feather (see Fig. 92).—Feather may appear in the shape of branch-

FIG. 90.—SILK FIBRES (× 500).

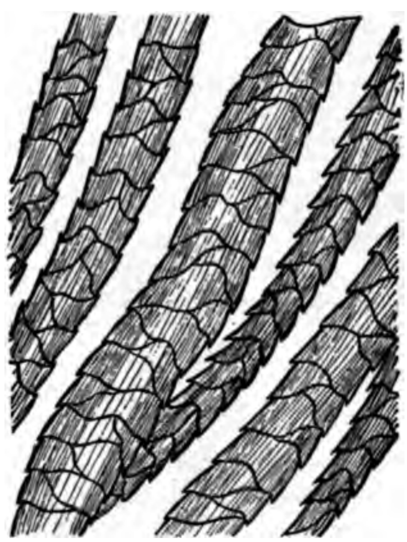

FIG. 91.—WOOL FIBRES (× 500).

ing formations, which have their origin at the quill, and run in different directions or in single barbules. The quill is striated. The barbules are composed of different sized links, and gradually taper toward the ends, which are whip-like.

FIG. 92.—FEATHER (× 400).

Scales from Moth (see Fig. 93).—Scales from the wings of insects, such as moths, may also be found. They are more or less delicate, serrated plates with a stem-like projection, and vary considerably in length and breadth.

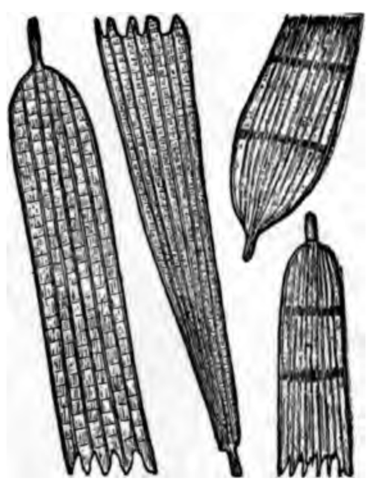

FIG. 93.—SCALES FROM WINGS OF MOTH (× 500).

Starch Globules (see Fig. 94).—Starch globules are frequently seen in the urine. They are more commonly found in the urine of females, starch powders being extensively used for dusting purposes, but individual globules from the underwear are also seen. They are oval or round, highly refractive, and vary greatly in size, with a more or less central hilum or umbilicus, around which are concentric striations. The hilum may be either round, oval, or irregular, at times quite large, at times small. and occasionally appearing as if split.

The different varieties of starch, although having the same characteristics, vary in shape as well as in size. The three most frequently found

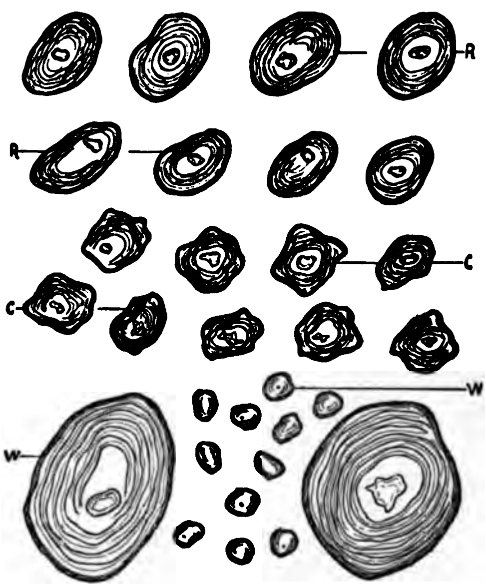

FIG. 94.—STARCH GLOBULES (× 500).
R, Rice starch; *C*, corn starch; *W*, wheat starch.

in the urine are rice starch, corn starch, and wheat starch. Rice starch always appears in the form of oval or oblong, quite regular globules of medium size. Corn starch is smaller, irregular, at times almost hexagonal, and contains an irregular hilum. Wheat starch consists of large globules, as well as of small, irregular formations, in which latter the hilum may be entirely absent or is present only in the form of a dot.

Lycopodium (see Fig. 95).—Lycopodium, somewhat similar to starch, and also considerably used for dusting purposes, consists of globular formations of different sizes, with a distinct shell, and studded with peculiar thorny projections. Many globules seen in urine are partially broken, and in some an irregular or triangular division is noticeable.

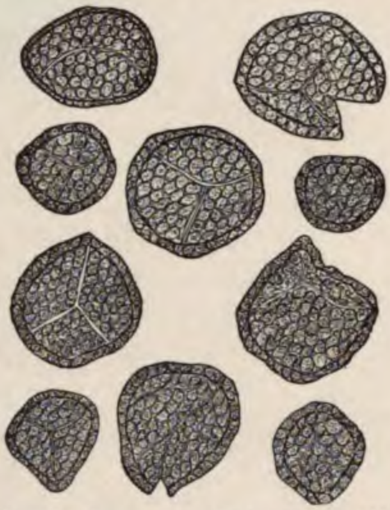

FIG. 95.—LYCOPODIUM GLOBULES (× 500).

Cellulose (see Fig. 96).—Cellulose occurs in the urine in a variety of forms, sometimes in small, sometimes in large masses. It varies considerably, according to the plant or portion of plant from which it is de-

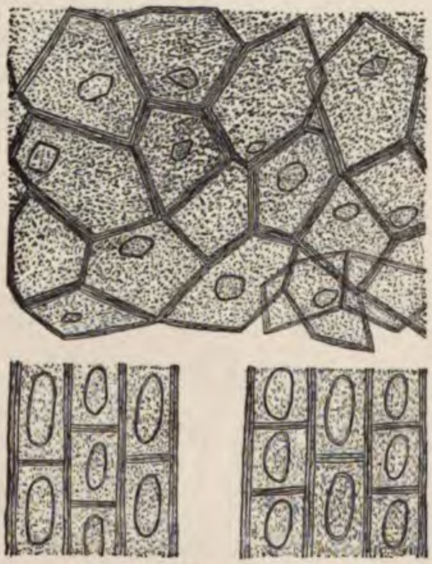

FIG. 96.—CELLULOSE (× 500).

rived, and may be brown, pale yellow, or practically colorless. It may be seen in the urine in the form of a framework, sometimes angular, the individual cells being connected with each other by the intercellular sub-

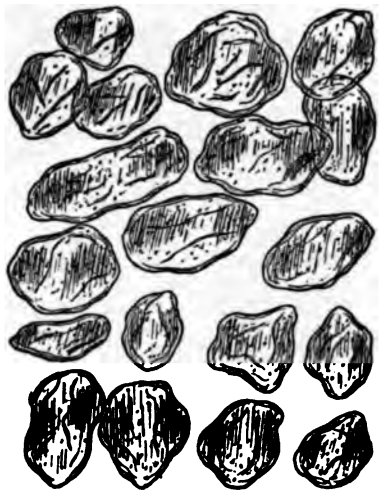

FIG. 97.—CORK (× 500).

stance. In the interior of many, though not in all, cells, a nucleus, usually somewhat irregular, is present, and both the cells and the nucleus are granular.

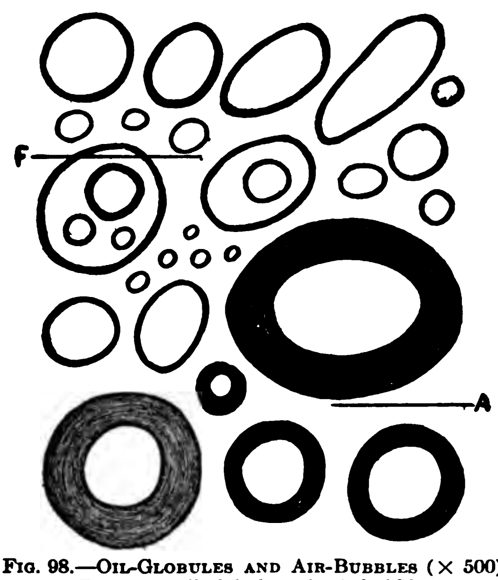

FIG. 98.—OIL-GLOBULES AND AIR-BUBBLES (× 500).
F, Fat- or oil-globules; *A*, air-bubbles.

Instead of the irregular angular cells, perfectly regular, either rectangular or square cells, with large, regular, oblong nuclei, may be seen, and these may also be found singly or in masses.

Cork (see Fig. 97).—A common variety of cellulose seen in urine is cork. This occurs either in single cells or smaller conglomerations, and has a yellowish-brown or reddish-brown color. The individual cells are irregular and greatly vary in size. They are either perfectly homogeneous or contain a small number of indistinct granules. At times many of these cells will be found closely packed together. When the cells are thin, they may possibly be mistaken for epidermal scales, but their color is always sufficient to differentiate them from the latter.

Oil-Globules and Air-Bubbles (see Fig. 98).—Extraneous fat- or oil-

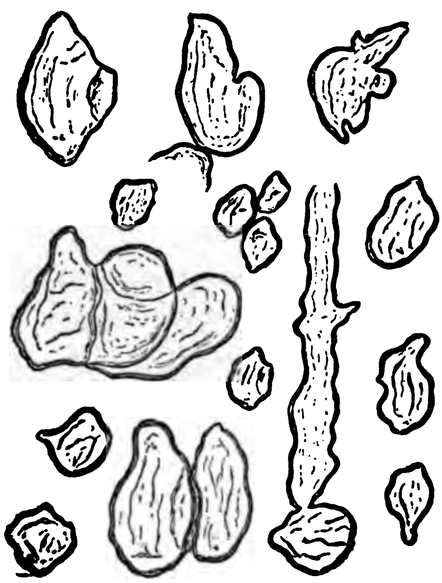

FIG. 99.—FLAWS IN THE GLASS (× 500).

globules are of common occurrence in urine. They may be very large or extremely small, and are either perfectly round or irregular. They are of a high refraction, and can frequently be differentiated by their yellowish color. The smallest globules might perhaps be mistaken for fat-globules voided with the urine, but are almost invariably associated with the larger, more irregular, yellowish globules.

Air bubbles also vary in size to a great degree, and may be either round or irregular; they have a sharply defined, double contour and a blue or bluish-black refraction.

Flaws in Glass (see Fig. 99).—Flaws in the glass, as well as scratches in the cover glass, may easily lead to a mistaken diagnosis. The flaws are irregular in size and shape, and frequently resemble the wings of a butterfly. They have a faint blue refraction and are usually pale. A lit-

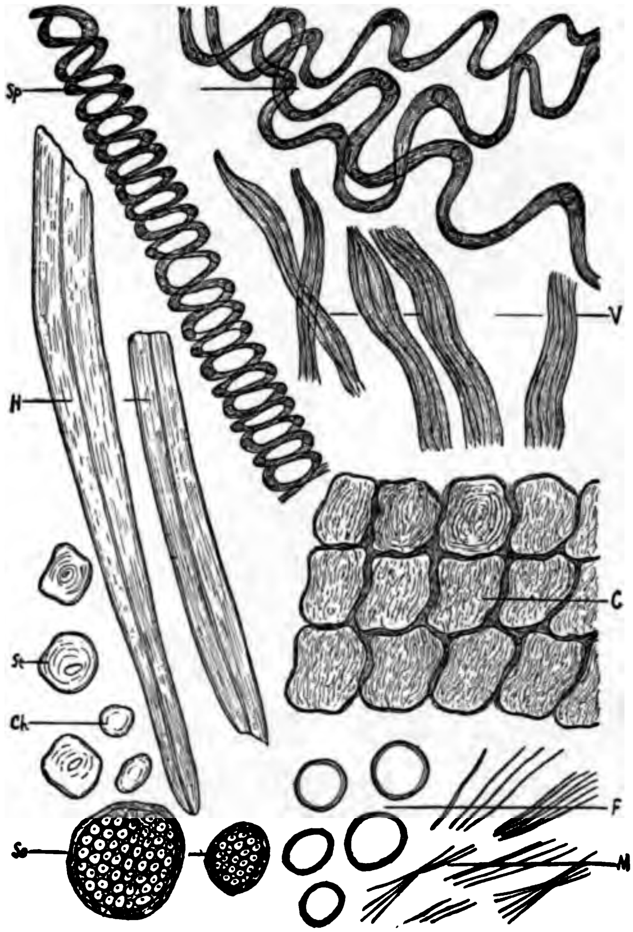

FIG. 100.—VEGETABLE MATTER (× 500).

Sp, Spiral fibres from air-vessels of plants; *V*, vegetable fibres; *H*, hairs of plants; *C*, cellulose; *St*, starch-globule; *Ch*, chlorophyl-globule; *F*, fat-globules; *M*, margaric-acid needles; *So*, spores.

tle care is sufficient to diagnose them; and if their identity is not plain, a change of the glass will suffice to note their character.

Rust particles in both the cover glasses and slides also occur, and are larger or smaller, dark or rust-brown, irregular masses, which must not be mistaken for coloring matter in the urine. The smaller masses somewhat resemble hæmatoidin crystals, but are always more irregular.

Vegetable Matter (see Fig. 100).—Vegetable matter of different forms may be found in the urine as an admixture from the fæces. Different

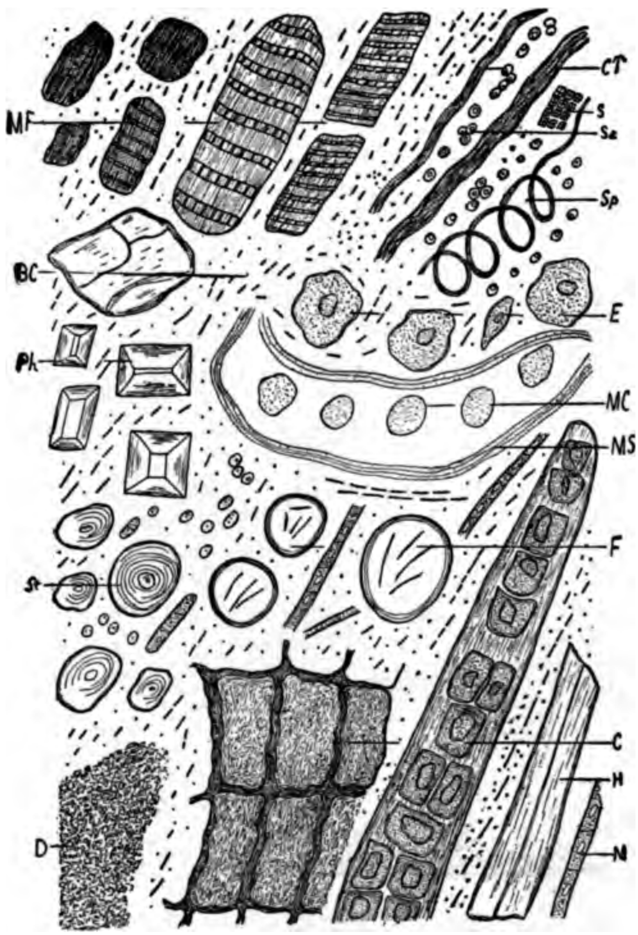

FIG. 101.—NORMAL FÆCES (× 500).

MF, Muscle fibres; *CT*, connective-tissue shreds; *Sp*, spiral fibre; *C*, cellulose; *H*, hair of plant; *MS*, mucus-thread; *MC*, mucus-corpuscle; *E*, epithelia; *Ph*, triple phosphates; *St*, starch-globules; *D*, débris; *M*, mycelium; *S*, sarcina; *Sa*, saccharomyces; *F*, fat-globules containing margaric-acid needles; *BC*, bacilli and cocci.

plants, which remain partially undigested and may be passed with the fæces in small masses, will present a variety of features. Spiral fibres from the air-vessels of plants are quite numerous in such masses. Hairs of plants, as well as vegetable fibres, the latter resembling connective-tissue shreds, will be found, besides particles of cellulose. We may furthermore see starch- and chlorophyl-globules, masses of spores, fat-globules, and margaric-acid needles.

Fæces (see Fig. 101).—Normal fæces may occasionally be found mixed with urine, and their constituents must be known. If they are present and their accidental admixture can be excluded, the diagnosis of a fistula can be made. Although their features vary greatly, depending upon the food, the most common with a mixed diet are the following:

Partly digested muscle fibres of a yellowish or brown color are almost constantly seen; in many the striations will be plainly visible, while in others no structure can be made out. Connective-tissue shreds from the meat diet, in small numbers, are also present. Spiral fibres, hairs of plants, and different forms of cellulose are almost constant ingredients, as well as starch- and chlorophyl-globules, and fat in the form of globules and needles.

Mucus-threads and mucus-corpuscles are usually found in normal fæces, as well as different varieties of epithelia. The latter are mostly of the flat variety, derived from the mucous membrane of the anus, although a few columnar epithelia are not rare. Crystals of various kinds, but most commonly triple phosphates, may be quite abundant. Different non-pathogenic bacteria, such as conidia and mycelia in small numbers (undoubtedly secondary products), saccharomyces, and large numbers of bacilli and cocci, may be found. Besides these features masses of débris, digested material, in smaller or larger conglomerations, will be seen.

The extraneous matters here enumerated as occurring in the urine are those which are more commonly found, but other features may be seen at one time or another. For instance, water fungi of different varieties, although rare, are known to occur in urine. It will, however, be a comparatively easy matter to recognize most of the extraneous objects.

PART THIRD.

MICROSCOPICAL URINARY DIAGNOSIS.

PART THIRD.

MICROSCOPICAL URINARY DIAGNOSIS.

ALTHOUGH it has been customary, in arriving at a correct diagnosis of diseases of the genito-urinary tract, to consider the microscopical examination of the urine as only of secondary importance, and, in diagnosing the different inflammations of the kidney, to rely solely upon the presence of casts, a perusal of the previous pages will show that the microscope is not only of the utmost importance in all these affections, but is frequently the only means of arriving at correct conclusions as to the nature of the case.

It is a well-known fact that in many cases in which a small amount of albumin is present in the urine, and in which the clinical symptoms seem to point to a nephritis, even if only slight, that diagnosis will not be made, because frequent examinations of the urine fail to reveal any tubular casts, and the physician is apt to rest satisfied with the diagnosis of "functional albuminuria"; yet a large number of not infrequently severe cases of nephritis exist which never show casts in the urine. In cirrhosis of the kidney, for instance, the presence of true casts is quite rare, and, when they are present at all, may be so scanty as to be entirely overlooked.

On the other hand, many cases of nephritis, often lasting for years, will give such ill-defined clinical symptoms that a kidney inflammation is rarely thought of; and the examination of the urine, if made at all, is done rapidly and merely with the idea of satisfying one's self that casts are not present. Many of these cases will show only a trace of albumin in the commencement stage, and might not only be greatly benefited, but entirely cured, if a proper diagnosis were made soon enough. Such a diagnosis can always be made from a microscopical examination of the urine, even without the presence of casts, and the larger number of the mild cases never show true casts in the urine at any time.

The diagnosis of an inflammation or other affection of the kidneys is undoubtedly the most important, but a microscopical examination of the urine may also be the only means of positively diagnosing the nature of a disease of the pelvis of the kidney, the bladder, and the prostate gland, as well as of clearing up a suspected case of inflammation of the seminal vesicles. In the female, an inflammation or ulceration of the vagina, the cervix uteri, and the mucosa of the uterus can often be positively identified from the examination of urine, without the necessity of an examination of the patient. It can thus easily be seen that the microscope plays an extremely important rôle in genito-urinary affections, either giving the first evidence of a disease or helping to clear up a doubtful diagnosis.

In the following pages only those affections will be considered which can be positively diagnosed from a microscopical examination of the urine.

CHAPTER XVI.

DISEASES OF THE KIDNEY AND PELVIS OF KIDNEY.

I. *INFLAMMATIONS OF THE KIDNEY AND ITS PELVIS.*

Classification.—There are probably no diseases in which the opinions of pathologists differ so much, and in which the nomenclature is so varied, as in inflammations of the kidney—nephritis. The result must necessarily be confusion. Such different terms as Bright's disease, interstitial, desquamative, exudative, parenchymatous, and diffuse nephritis are met with, and congestion or hyperæmia, glomerulitis, pyelo-nephritis, and amyloid disease are all looked upon as different affections. While some authors use the term Bright's disease as indicating all the different varieties of nephritis, others call diffuse nephritis *Morbus Brightii;* others, parenchymatous nephritis; and still others, combinations of different varieties.

A uniform classification of nephritis is difficult, since various phases of inflammation and degeneration are closely associated and often merge, and some authors separate a number of these different phases. One classification* is the following: 1. Acute parenchymatous nephritis or acute Bright's disease. Varieties of this form are acute degenerative nephritis, acute catarrhal or desquamative nephritis, acute glomerulonephritis, acute diffuse nephritis, to which belongs the hemorrhagic form. 2. Acute interstitial nephritis, non-suppurative in character, and suppurative nephritis. 3. Chronic parenchymatous nephritis; to this form belong chronic diffuse and chronic hemorrhagic nephritis, also the large white kidney. Its terminal form is known as fatty contracting kidney or secondary interstitial nephritis. 4. Chronic interstitial nephritis, divided into primary chronic interstitial or red granular kidney or arteriosclerotic nephritis or gouty nephritis, and secondary chronic interstitial, the terminal form of chronic parenchymatous nephritis.

Delafield and Prudden† mention three principal varieties of inflammatory processes of the kidney: 1. Acute suppurative nephritis. 2. Acute diffuse nephritis. 3. Chronic diffuse nephritis. The variations in

* Stengel and Fox, "Textbook of Pathology," 6th Edition, 1915.

† "Text-Book of Pathology," 11th Edition, 1919.

type in acute diffuse nephritis are the following: (*a*) Glomerulo-nephritis; (*b*) parenchymatous or degenerative type; (*c*) hemorrhagic type; (*d*) exudative type; (*e*) productive type or interstitial type. Variations in type in chronic diffuse nephritis are: (*a*) Parenchymatous or degenerative type; and (*b*) interstitial type.

Adami and McCrae* divide nephritis into acute interstitial, acute parenchymatous, chronic interstitial and chronic parenchymatous. Of these, all but the first are called Bright's disease; in the first, exudative changes are the most prominent, in the last three, degenerative. Suppurative nephritis is an advanced form of acute interstitial.

It is unnecessary to go any further into the different classifications, which no two authors give alike, but it may be mentioned that some prefer to speak primarily of an acute and a chronic nephritis only, dividing them into parenchymatous and interstitial secondarily.

It is, therefore, not at all surprising that the pathology of nephritis is considered to be one of the most complicated chapters in pathology; yet it will become perfectly plain, and the features found in urine easily explained, if we consider the anatomical structure of the kidney, which is that of a compound tubular gland, consisting of epithelial and connective tissue; the latter alone carries the blood-vessels, the contents of which, the blood, furnish the material from which the epithelia produce the secretions.

Experiments have frequently been made to show that pathological conditions of the epithelia can exist independently of the underlying connective tissue carrying the blood-vessels. It has been asserted that in acute cases of poisoning, such as with cantharides and phosphorus, the pathological process is confined to the kidney epithelia alone. Other experiments have, however, conclusively proved that an independent pathological condition of the epithelia does not exist. The poison, before it reaches the epithelia, must pass the walls of the blood-vessels and the connective tissue lying between the epithelia and the walls of the blood-vessels, and has an irritating influence upon the latter. In this connective tissue, changes are always found, though they may be confined to serous transudation, sufficient to show that the epithelium cannot become diseased primarily and independently of the surrounding connective tissue.

It is, therefore, evident that the classification by Virchow, of inflammations into *interstitial*, that is, confined to the connective tissue, and *parenchymatous*, confined to the epithelia, is not strictly correct. Every inflammation is primarily an interstitial one, and every parenchymatous

* "Text-book of Pathology," 2nd Edition, 1914.

inflammation must also at the same time be an interstitial one. It is perfectly true, however, that the pathological changes may be more pronounced in the epithelia than in the connective tissue; the latter may not pass beyond the stage of serous infiltration, while in the former coarse granulation, so-called cloudy swelling, may occur. In cases of phosphorus poisoning fatty degeneration may be present.

The character of an inflammation depends to a great degree upon the nature of its exudate, which may be either serous, fibrinous, or albuminous. In former years inflammations of mucous membranes were divided into *catarrhal* and *croupous;* in the first a serous or sero-mucous exudate is formed, while in the second it is fibrinous in its character. These names, though not of great significance, are perhaps preferable to Virchow's terms—interstitial, desquamative, and parenchymatous—which, as has been shown, cannot be carried out. An inflammation in an organ composed of connective and epithelial tissue will affect all its component parts to a greater or less degree, so that it will be diffuse to a certain extent at the outset. The difference exists only in the degree in which the different tissues are affected. We may, if we wish, speak of an interstitial inflammation when the pathological changes are more pronounced in the connective tissue, and of a parenchymatous inflammation when they are more pronounced in the epithelia.

As every inflammation of the kidney is bound to be more or less diffuse in its character—by which term is not meant that it affects the entire organ uniformly, but simply all the component parts of the organ at the seat of inflammation—and the term Bright's disease conveys no meaning as to the character of the inflammation, which may run an acute, subacute, or chronic course, all cases of nephritis may best be divided in the following manner:

1. Interstitial, catarrhal, or desquamative nephritis.
    (*a*) Acute.
    (*b*) Subacute.
    (*c*) Chronic, terminating in cirrhosis of the kidney.
2. Parenchymatous or croupous nephritis.
    (*a*) Acute.
    (*b*) Subacute.
    (*c*) Chronic, terminating in atrophy of the kidney.
3. Suppurative nephritis.
    (*a*) Acute.
    (*b*) Chronic.

When the greater part or the entire kidney is transformed into a purulent cavity, the term pyonephrosis is applied.

Congestion or hyperæmia of the kidney cannot be considered as a separate affection, since it is either the first stage of a commencing inflammation or a mere irritation, which cannot be properly termed inflammatory as yet, but which sooner or later will undoubtedly develop into an inflammation.

Glomerulitis or glomerulo-nephritis is not an independent inflammatory process, but only a symptom of one of the inflammations, since the glomeruli are always attacked to a greater or less degree in every nephritis.

Fatty and waxy, or amyloid, degenerations of the kidney are almost invariably secondary products, due to a chronic inflammation, and part of such an inflammation.

Pathological Changes.—Let us now briefly consider the pathological changes which take place in these different inflammations of the kidney:

1. *Interstitial Inflammation.*—In interstitial or catarrhal inflammation of a mild character, an œdematous swelling of the connective tissue is present, with swelling and granular cloudiness of the epithelial covering and subsequent desquamation of the epithelium. The blood-vessels show a more or less complete distention with blood-corpuscles, without apparent alteration in the structure of their walls. The œdematous swelling of the connective tissue, as well as the desquamation of the epithelia, is due to a serous exudation from the blood-vessels. On account of this serous exudation, the epithelia may undergo degenerations.

In severer cases an inflammatory infiltration of the connective tissue, which leads to hypertrophy, takes place, with proliferation, desquamation, and, finally, hyperplasia of the epithelium. In the highest degree of catarrhal inflammation, all the constituent parts of the kidney tissue have disappeared in the inflammatory infiltration.

At the very commencement of an inflammation, the production of pus-corpuscles takes place, partly from the emigration of white blood-corpuscles, partly from the interstitial connective tissue and partly from the epithelium, which latter undoubtedly enters into the formation of pus-corpuscles to a great degree by division and endogenous cell-proliferation, as had already been shown by George Johnson, in the year 1852. As long as the newly formed corpuscles remain in connection with the tissue, we have inflammatory corpuscles; but as soon as they are torn from their connection with the tissue and appear in the urine, the term pus-corpuscles must properly be applied to them.

When the disease has become chronic, the surface of the kidney is marked by irregular, shallow depressions, or by granulations, the capsule being adherent in most cases. The irregular depressions are due to retractions of newly formed connective tissue, which is formed at the expense of the uriniferous tubules. Chronic catarrhal or interstitial nephritis invariably leads to a shrinkage—*cirrhosis*—of the kidney. The whole kidney is considerably reduced in size, and the irregularities on the surface are well marked. Both the cortical and medullary substances are much narrower than in the normal condition; this being more particularly the case in the cortex, of which, in advanced stages, only slight remnants are left, corresponding with the elevations of the surface. There is a partial destruction of tufts or glomeruli, tubules, and blood-vessels. The newly formed connective tissue is more or less regularly distributed throughout the kidney structure, the uriniferous tubules being in part transformed into connective tissue, while still retaining the outlines of their original configuration.

The obliteration of a number of the narrow tubules, including the ascending and descending branches, explains the clinical fact that persons affected with cirrhosis of the kidney void large quantities of urine almost destitute of salts. It is well known that from the glomerulus only a watery liquid, containing few salts, is voided, which becomes thicker by the addition of the saline constituents excreted by the narrow tubules. It is in the narrow tubules that much of the watery part of the urine is restored to the thickened blood running in the neighboring capillaries. If the function of the tubules be much interfered with, the interchange between the liquid contents of the tubule and the solid constituents of the blood will not take place, and consequently the urine will be voided in about the same condition in which it was pressed into the capsule from the tuft. Numbers of the convoluted tubules perish also through the increased formation of connective tissue, while from others the epithelia are simply desquamated and appear in the urine.

2. *Parenchymatous Inflammation.*—In parenchymatous or croupous inflammations the surface becomes partially or completely denuded of its epithelium, a coagulated albuminous or fibrinous exudate is formed upon the surface, there is considerable hyperæmia of the blood-vessels, as well as a pronounced swelling and inflammatory infiltration of the connective tissue. Undoubtedly the epithelia enter very actively in the formation of the so-called croup membrane, and their protoplasm becomes almost completely destroyed in the fibrinous exudate.

In this variety of inflammation the emigration of colorless blood-corpuscles is quite pronounced. Epithelia alone cannot produce a croup membrane, but require the presence of an exudate from the blood, and the essential constituent of the croup membrane is the coagulable albuminoid body from the blood. We now have the formation of casts; the epithelia lining the tubules become saturated with the albuminous exudate, swell, grow pale, and finally, by coalescence of the epithelia thus degenerated, produce the mass called a tubular cast.

In chronic parenchymatous nephritis the kidney has an entirely different appearance from that found in chronic interstitial nephritis and cirrhosis of the kidney. It is more frequently enlarged than diminished in size. The surface is often nodulated, and between the nodules are seen deep cicatricial retractions. These retractions are never found uniformly over the surface, and the capsule is adherent to the retractions. The cortical substance is absent in those parts corresponding with the retractions of the surface, while in other places the cortex may be unaltered or even increased in bulk. The pyramidal substance may be unchanged or may be diminished. In contradistinction to the more or less uniform shrinkage of the kidney, to which the name *cirrhotic* is given, the partial destruction of the tissue which occurs in chronic parenchymatous nephritis may be termed *atrophy*, since in the most diseased portions only traces of the original kidney structure are left.

In the depressed cicatricial portions of the cortical substance a large amount of connective tissue, only scantily supplied with blood-vessels, is found. There is no regularity in the arrangement of the connective tissue, and only remnants of the former tubules are found, together with irregularly scattered sections of tubules, from which the epithelial lining has entirely disappeared. In the most pronounced cases, in addition to the atrophied portions, the large amount of newly formed connective tissue present in different places constitutes a regular hypertrophy.

Both fatty and waxy degeneration may be present in cirrhotic as well as in atrophied kidneys, but these changes are much more pronounced in the latter than in the former. In the so-called large white kidney, the highest degree of fatty degeneration occurs as a secondary result of chronic parenchymatous nephritis. Cystic degeneration may also be present in these cases, and is more pronounced in chronic parenchymatous nephritis.

3. *Suppurative Inflammation.*—The most intense variety of inflammation of the kidney is the suppurative, which is similar to the formation of suppuration in other organs. It is a distinctly different process from the purely interstitial type although some authors consider it an advanced form of interstitial. In it there is an excessive emigration of polymorphonuclear leucocytes together with a liquefaction of the different tissues. Many blood-vessels soon become destroyed. In the formation of pus a disintegration of tissue occurs, and all the elements of the tissue take part.

There may be either a number of small disseminated foci of suppuration or a large abscess, usually, if not invariably, caused by an invasion of pyogenic cocci. Besides the abscess, the kidney may present the features either of an interstitial or of a parenchymatous inflammation. When the abscesses become chronic, a dense connective-tissue capsule, the pyogenous membrane, may occasionally be found, and the pus becomes inspissated into a cheesy mass.

With these remarks upon the pathology of the different varieties of nephritis, we are ready to understand the features found in the urine of these cases. Although it is not possible to diagnose an acute, subacute, or chronic inflammation from the urine alone, in all cases of nephritis, it can undoubtedly be done from the different features seen in most cases, especially the more pronounced.

CONGESTION OR HYPERÆMIA OF THE KIDNEY.

From what has been said before, it is evident that the diagnosis of an inflammation can be made as soon as pus-corpuscles are found in the urine; without these, no such diagnosis is possible. In some cases, in which a trace or faint trace of albumin is present, an extremely small number of pus-corpuscles or rather leucocytes, perhaps one or two in every field of the microscope, is seen, together with the same number of epithelia from the uriniferous tubules, and a few red blood-corpuscles. These features, when present in such very small numbers, are not sufficient for the diagnosis of an inflammation, though the urine cannot be called normal. In such cases the diagnosis of a *congestion or hyperœmia of the kidney* is possible, and in them we do not, as a rule, find true casts. In severe cases a few hyaline casts may be found, and red blood-corpuscles are somewhat more numerous. In such cases a differentiation between congestion and inflammation may be difficult.

In some cases of congestion mucus-threads and cylindroids, which latter can sometimes hardly be distinguished from hyaline casts, may be present, this being especially the case in acute eruptive and inflammatory diseases, such as scarlatina, diphtheria and pneumonia. The color, amount of urine and specific gravity may be normal in mild cases; in severe cases the urine is highly colored, the quantity diminished and the specific gravity high. In chronic cases fat globules are present.

Causes.—Congestion of the kidney is of common occurrence, but is frequently overlooked. It may be present accompanying almost any disease, and may be produced by different medicinal agents, such as cubebs, copaiba, turpentine, cantharides, and mineral acids. Occasionally it seems as if simple exposure to cold and moisture is sufficient to produce it. In cases of catarrhal or gonorrhœal urethritis, especially if accompanied by slight prostatitis, an irritation of the kidney is often found, giving the features enumerated above. The presence of an increased amount of salts, such as uric acid or calcium oxalate, will not infrequently be responsible for the condition.

If the cause which has produced the congestion be quickly removed, the affection may disappear at once; but if not, an inflammation will sooner or later result.

If the congestion is pronounced, a more or less severe *hemorrhage from the kidney* may take place, even without an inflammation. In such cases red blood-corpuscles will be numerous, epithelia from the convoluted tubules may be somewhat more abundant, and, in addition, scanty, delicate shreds of connective tissue will appear in the urine. All the features may have a yellowish hue from the coloring matter of the blood.

INTERSTITIAL OR CATARRHAL NEPHRITIS.

Interstitial, catarrhal, or desquamative nephritis frequently runs a comparatively mild course, being, as a rule, the mildest of the three varieties of inflammation. Severe acute cases, which may cause the death of the patient, do, however, occur. Interstitial nephritis is a much more common affection than is generally supposed, and may exist for many years without giving any pronounced clinical symptoms. It is by no means rare that a urine which is examined microscopically with a view of detecting other affections will show the presence of such an inflammation before the clinical symptoms are clear, though the patient may have suffered for a long time from occasional headaches and general depression.

Causes.—Interstitial nephritis often exists in a mild degree without any known cause. Exposure to cold and moisture seems to be a frequent cause, as are also different medicinal agents, such as arsenic, iodine, phosphorus, mercury, turpentine, and cantharides. In lead-poisoning the disease is often present. It is not infrequently found in persons of sedative habits and in those with a so-called gouty or rheumatic diathesis. That persons suffering from gout and rheumatism usually void a large amount of uric acid is well known; but there are others who continually void uric acid and calcium oxalate in excess without giving any rheumatic symptoms. In these cases—lithæmia and oxaluria—interstitial nephritis frequently occurs, and it seems that the excess of the salts, or the concentration of the urine itself, has an irritating tendency upon the kidney tissue. The continued use of alcohol is an important factor in the production of the disease.

In acute contagious diseases parenchymatous nephritis is of more common occurrence than interstitial, but the latter, contrary to the general belief, undoubtedly occurs. If the urine is carefully examined in these diseases, a small amount of albumin, perhaps not more than a trace, may be found in the milder cases, and upon microscopical examination the features of an interstitial inflammation are seen. Even in some fatal cases, an examination of the kidney may reveal an interstitial and not a parenchymatous inflammation. In pregnancy, also, interstitial nephritis occurs, and is not at all rare.

As a secondary affection, this variety of inflammation may be present in many acute and chronic fatal diseases, so much so that, upon post-mortem examinations, absolutely healthy kidneys are usually found only after death by accident.

Finally, interstitial nephritis is common as a result of various genito-urinary affections, as, for instance, in some cases of gonorrhœa, when first a prostatitis, then, in succession, a cystitis, pyelitis, and nephritis will develop. In syphilitic and tubercular affections it is frequently seen.

Clinical Symptoms.—The clinical symptoms of the disease vary greatly, but in the milder cases are anæmia, occipital headache, pain in the lumbar region, loss of appetite, sleeplessness, and general depression. In cirrhosis of the kidney the symptoms are pronounced, loss of flesh and strength is well marked, vomiting may be frequent, there may be dyspnœa, and the pulse is tense, hard, and often full. The acute cases may occur at any age, but the chronic cases are mostly found in persons more advanced in years, especially after the age of forty years.

Features Found in Urine.—Albumin, although present in most of the cases, may be found in very small amount only, and in some it seems to be entirely absent. A large amount of albumin is rare in interstitial nephritis, and is seen only in the severe cases. In many, a trace of albumin only will be found, and unless a careful observation is made, it may escape detection entirely. The question whether a pronounced inflammation of the kidney may exist with entire absence of albumin is still an open one. Many authors claim that it does occur, but many times when albumin is said to be absent careful examination will show a trace. It is undoubtedly a fact that in interstitial nephritis albumin may be absent at certain times, but frequent examination will almost invariably show at least a trace in every case.

The specific gravity, amount, and appearance of the urine will vary greatly. In milder cases these may be perfectly normal. In acute interstitial nephritis the specific gravity is, as a rule, somewhat higher than normal, the amount slightly decreased, and the color darker. The amount of urea is usually increased, and salts may be present in rather large numbers. In chronic cases the amount of urine is invariably increased, sometimes to a great degree; the specific gravity is low and the color pale. In such cases the specific gravity is not infrequently below 1.012 or 1.010

continually, the amount of urea and salts being diminished. The sediment found in the urine varies, but is usually small, and may at times be no more abundant than in normal urine.

A positive diagnosis of interstitial or catarrhal nephritis is in many eases possible only by a microscopical examination of the urinary sediment. This will vary in acute, subacute, and chronic cases. The diagnosis of a nephritis can be made when pus-corpuscles and epithelia from the convoluted and narrow tubules of the kidney are present in the urine. Columnar epithelia from the straight collecting tubules are of rarer occurrence, and indicate an invasion of the pyramidal substance.

Before the presence of epithelia from the convoluted tubules of the kidney can be diagnosed, pus-corpuscles must be found and taken as a standard, since the latter vary in size to a certain degree in every given case. Kidney epithelia from the convoluted tubules are about one-third larger than the pus-corpuscles. These epithelia are never found in normal urine, and to render their diagnosis positive, they should always be compared with pus- or white blood-corpuscles. A single kidney epithelium is of no value for the diagnosis, and a small number, at least, should always be found, in order to render the diagnosis positive, since, as is well known, pus-corpuscles vary in size to a small degree even in the same case. This difference is, however, small, and never so pronounced as to render the diagnosis between pus-corpuscles and kidney epithelia difficult. The difference in size between the two can alone determine the nature of the epithelia, since the presence or absence of a nucleus has no significance whatever. A nucleus may be seen in pus-corpuscles, as well as in epithelia, though it is found more frequently in the latter than in the former. In finely granular pus-corpuscles a nucleus will always be visible, while in coarsely granular epithelia it may not be seen.

Kidney epithelia from the convoluted as well as those from the narrow tubules generally have a round shape in urine, though angular or irregular forms are also seen. When the urine is still warm at the time of examination, or in a warm temperature, the pus corpuscles may not infrequently show amœboid movement and assume a variety of different shapes, while the kidney epithelia, as a rule, retain their round or slightly irregular form.*

In this variety of nephritis casts are usually absent; if they are present at all, they are found in extremely small numbers, and then we almost

* Attention should here again be called to the fact that low magnifying powers of 100 or 150 diameters are absolutely useless for a diagnosis of kidney epithelia. A magnifying power of at least 400 diameters must be used, and with such a power the difference between pus-corpuscles and kidney epithelia becomes apparent at once.

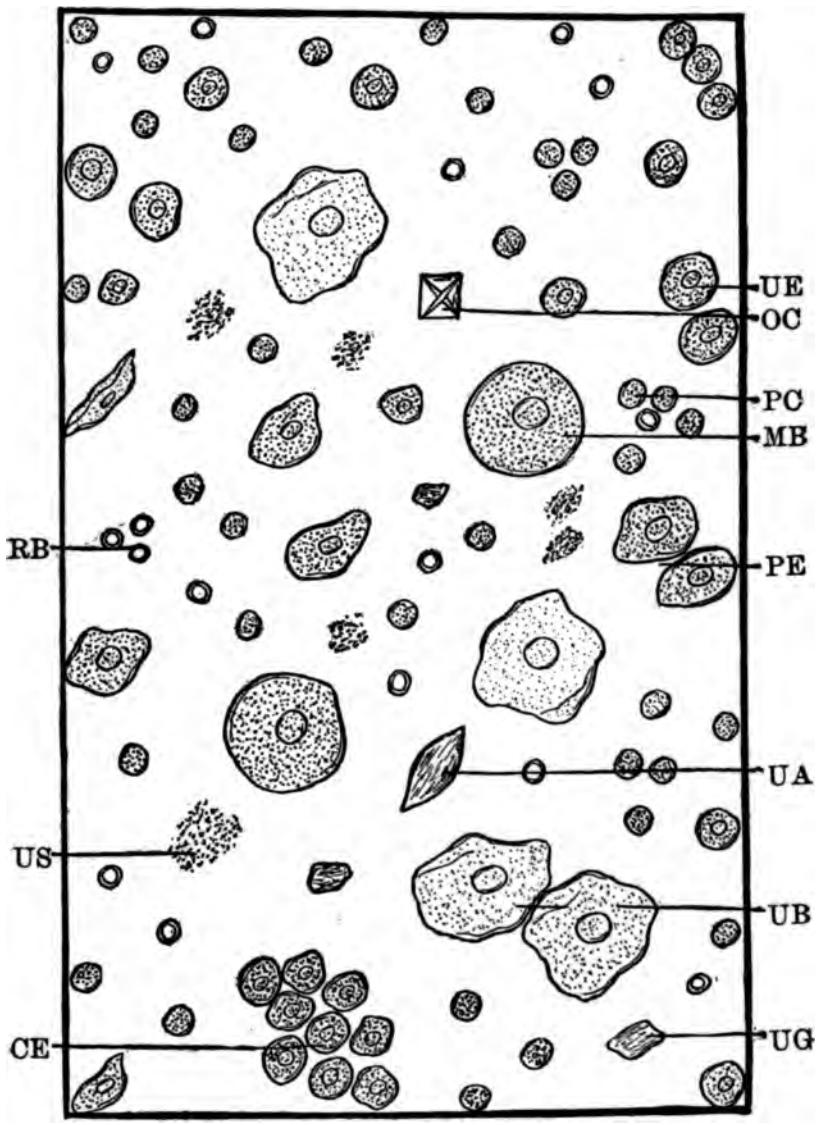

FIG. 102.—ACUTE INTERSTITIAL NEPHRITIS (ACUTE CATARRHAL PYELO-NEPHRITIS) AND CYSTITIS (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles; *CE*, epithelia from the convoluted tubules of the kidney; *UE*, epithelia from the ureter; *PE*, epithelia from the pelvis of the kidney; *UB*, epithelia from the upper layers of the bladder; *MB*, epithelium from the middle layers of the bladder; *UA*, uric acid; *UG*, uric-acid gravel; *US*, sodium urate; *OC*, calcium oxalate.

invariably see small hyaline casts from the narrow tubules only. The diagnosis, however, hinges upon the presence of epithelia from the convoluted and narrow tubules and pus corpuscles, together with other features to be presently mentioned.

Acute Interstitial or Catarrhal Nephritis (Fig. 102).—In an acute interstitial nephritis the pus-corpuscles and cuboidal epithelia from the convoluted tubules of the kidney are present in at least moderate but usually large numbers; the more numerous these features, the severer is the nephritis. Besides these, we usually find red blood-corpuscles in moderate or fairly large numbers, though they are not sufficiently numerous to admit of the diagnosis of a hemorrhage. Moderate numbers of red blood-corpuscles always indicate an acute inflammation.

These three features are perfectly sufficient for the diagnosis, but are rarely found alone. In many cases different salts, such as calcium oxalate, uric acid, and sodium urate, are found in small amount. In the severer cases a few columnar epithelia from the straight collecting tubules are also present. As a general rule, an inflammation of the pelvis of the kidney is associated with the nephritis, though this may be absent. When present, the irregular, lenticular, pear-shaped, or angular epithelia from the pelvis are also seen in varying numbers, and the diagnosis of a *pyelo-nephritis* can be made. Such a diagnosis does not by any means suggest an abscess of the kidney, as is frequently supposed, but simply the extension of the inflammatory process to the pelvis of the kidney. Besides these, epithelia from the ureters in small numbers, which are about twice the diameter of pus-corpuscles, and therefore larger than the kidney epithelia, are rarely absent.

If the nephritis is at all pronounced, symptoms of an accompanying cystitis are also seen, and we will then find larger cuboidal epithelia from the middle layers of the bladder—which in urine appear round or oval in most cases—as well as flat epithelia from the upper layers with the other features.

The severer the acute inflammation the more abundant are the accompanying features of pyelitis and cystitis. In such severe cases hyaline casts from the narrow tubules are occasionally present; if these are seen in small numbers only, the diagnosis does not necessarily become changed. The latter feature is comparatively rare, and in most cases casts of any kind are entirely absent.

Chronic Interstitial or Catarrhal Nephritis (Fig. 103).—As soon as the inflammation has become chronic, the features in the urine are different. Red blood-corpuscles are now either entirely absent, or, when present, are found in small numbers only. We observe, however, a varying number of small, glistening, highly refractive globules and granules, partly lying free, partly in the pus-corpuscles and epithelia. These are fat-globules and -granules, and the more numerous they are the more chronic is the inflammation. They are found in larger or smaller groups scattered throughout the field, and are seen in varying numbers in the pus-corpuscles and epithelia. In milder cases only two or three may be present in some epithelia, while they are absent in others; but in the old, chronic cases almost every epithelium will be seen filled with the glistening globules. When very numerous, they not only denote chronicity, but also a commencing fatty degeneration of the kidney, which, in this variety of nephritis, is never pronounced. Fat-globules are not seen in acute cases.

The features found in a chronic interstitial nephritis are, therefore, the following: Pus-corpuscles, some containing fat-globules and -granules; cuboidal epithelia from the convoluted tubules of the kidney, a few, or a large number, containing fat-globules; free fat-globules in different groups; in the severer cases, also, columnar epithelia from the straight collecting tubules, usually in small numbers only. Irregular or round epithelia from the pelvis of the kidney, cuboidal (round) epithelia from the ureters, and still larger cuboidal epithelia from the middle layers of the bladder, either with or without fat-globules, may be present in small or moderate numbers. A few granular casts may be seen.

Another feature of chronicity which may occasionally be found is hæmatoidin, in the form of rust-brown needles and plates. These may either lie free or when of small size may be seen in the pus-corpuscles and epithelia. They denote a previously existing hemorrhage, and show that the pathological process cannot be an acute one.

Red blood-corpuscles, as previously mentioned, are either entirely absent in a strictly chronic case, or, when present, are found in small numbers only. Not infrequently, however, all the features of a chronic inflammation are seen, and yet blood-corpuscles are fairly numerous. This invariably denotes a fresh acute outbreak engrafted upon the chronic process. Such acute attacks are not rare in cases of long standing, and may be produced by the slightest cause, such as exposure to cold, derangements of digestion, etc. Again, the chronic inflammation may be confined to one kidney and an acute process affect the second kidney.

In Subacute Interstitial Inflammations some features of both the acute and the chronic form will be found. We have a small or moderate number of red blood-corpuscles and a small number of fat-globules, the latter being rarely seen in groups, but only in a few pus-corpuscles and epithelia, and there may be only one, two, or three in them. The other features remain the same.

When the features as here described are present, it will not be difficult to tell whether an inflammation is acute, subacute, or chronic; but some

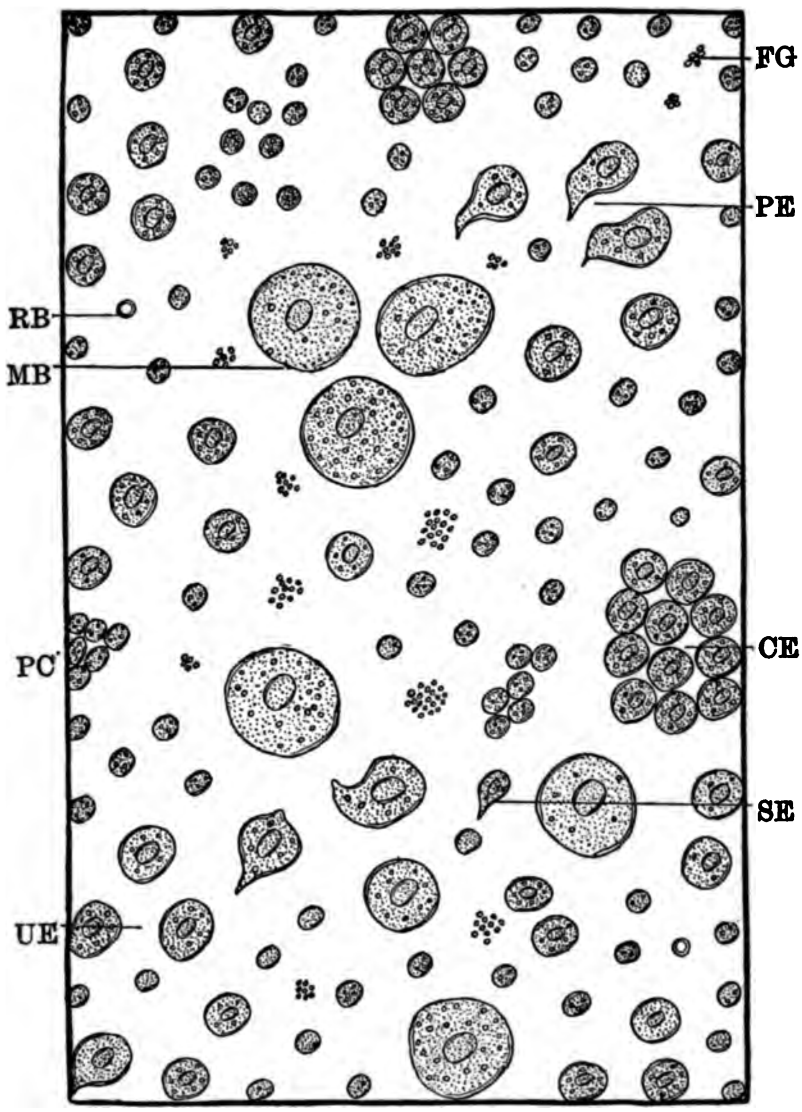

FIG. 103.—CHRONIC INTERSTITIAL NEPHRITIS (CATARRHAL PYELO-NEPHRITIS) AND CYSTITIS (× 500).

PC, Pus-corpuscles containing fat-globules; *CE*, epithelia from the convoluted tubules of the kidney containing fat-globules; *SE*, epithelium from the straight collecting tubules of the kidney containing fat-globules; *UE*, epithelia from the ureter containing fat-globules; *PE*, epithelia from the pelvis of the kidney; *MB*, epithelia from the middle layers of the bladder; *FG*, free fat-globules; *RB*, individual red blood-globule.

cases may at times be seen where neither red blood-corpuscles nor fat-globules can be discovered, and then the diagnosis of a simple interstitial or catarrhal nephritis can alone be made. These cases are usually of a mild character.

The severity of the inflammation as well as its duration can be determined more readily by the urinary features than by the clinical history, which may be vague. The less marked the features after repeated examinations of the twenty-four hours' mixture, the less severe the case is liable to be. The more abundant the fat globules both in the pus-corpuscles and in the epithelia and the more marked free groups of fat globules are, the more chronic is the inflammation.

Cirrhosis of the Kidney (Fig. 104).—The outcome of chronic interstitial nephritis is always a shrinkage—cirrhosis—of the kidney, the so-called hob-nail kidney. The features of this, as seen in the urine, are so characteristic that a positive diagnosis can always be made. They are the following:

1. A large amount of urine, being occasionally increased to double the normal quantity or more, and the color being pale.
2. A continuously low specific gravity, usually below 1.012 or 1.010, or even not more than 1.006 or less at any time.
3. The presence of a small amount or perhaps not more than a trace of albumin.
4. A diminution of all salts.
5. Pus-corpuscles, present in small numbers, some containing fat-globules.
6. Epithelia from the convoluted and straight collecting tubules of the kidney, in small numbers, some or even all containing fat-globules.
7. Free fat-globules and -granules.
8. Connective-tissue shreds, of small sizes and in small numbers only.
9. A few granular and also fatty casts. Such casts need, however, not necessarily be present and in many cases of cirrhosis no true tube-casts whatever are found.

Epithelia from the pelvis of the kidney, the ureter, and the middle layers of the bladder may also be present.

As previously explained, urine from a badly diseased kidney contains few salts. In some cases, in which all the other features of a cirrhosis are present, a large amount of salts, such as uric acid or phosphates, is also seen, the specific gravity being 1.014 or higher. The conclusion which can then be reached is that only one kidney has so far become affected, the salts being voided by the other kidney. The prognosis will, in such cases, be better than when salts are not seen under the microscope.

Catarrhal Pyelitis.—A few words should here be said about catarrhal pyelitis, which may occur as a primary or as an ascending affection. It has been claimed that the term "catarrhal" for an inflammation of the pelvis of the kidney is incorrect. As these inflammations, however, have undoubtedly the character of catarrhal processes,* we can speak of catarrhal pyelitis, just as of catarrhal nephritis.

When pyelitis occurs as such, it is easily diagnosed from the urine, the features being the same as in interstitial nephritis, except that pelvic epithelia instead of kidney epithelia are found. Being in many cases due to an abundance of salts, these will usually be present in such cases. Not infrequently, pyelitis is an accompanying element of a nephritis, giving us a catarrhal pyelo-nephritis, with the features as above described

Ureteritis.—A primary, independent inflammation of the ureter is rare, a ureteritis being almost invariably secondary to a pyelitis or a cystitis. It may be caused by infections of any kind or may be due to impacted calculi. In a catarrhal inflammation the same features as those seen in nephritis and pyelitis are seen, except that epithelia from the ureter alone are found. Ulceration and suppuration may also occur, giving features similar to those seen in ulcerative and suppurative conditions to be described in other organs. In the latter processes, however, columnar epithelia are present. In injury to the ureter due to the ureteral catheter, red blood-corpuscles, small cuboidal and columnar epithelia, and connective-tissue shreds are seen in the urine.

PARENCHYMATOUS OR CROUPOUS NEPHRITIS.

Parenchymatous nephritis is usually a severer affection than the interstitial, and is not quite as frequent as the latter. When present, its symptoms are always more or less pronounced, and only in rare cases will it exist for some time without giving symptoms sufficiently characteristic to suspect a nephritis.

Causes.—Its causes are numerous, being partly the same as those found in the interstitial variety. Exposure to cold and moisture is a common cause, and it is not infrequently the consequence of irritant poisons acting upon the system, such as turpentine, bichloride of mercury, cantharides, arsenic, large doses of iodide of potash, and occasionally even chlorate of potash. As in interstitial nephritis, it may be found in persons of a sedative habit and in those suffering from a lithæmia. The continued use of alcohol is an important causative factor.

Among the most common causes in the production of the disease are

* Adami and Nicholls. The Principles of Pathology, Vol. II, 1909.

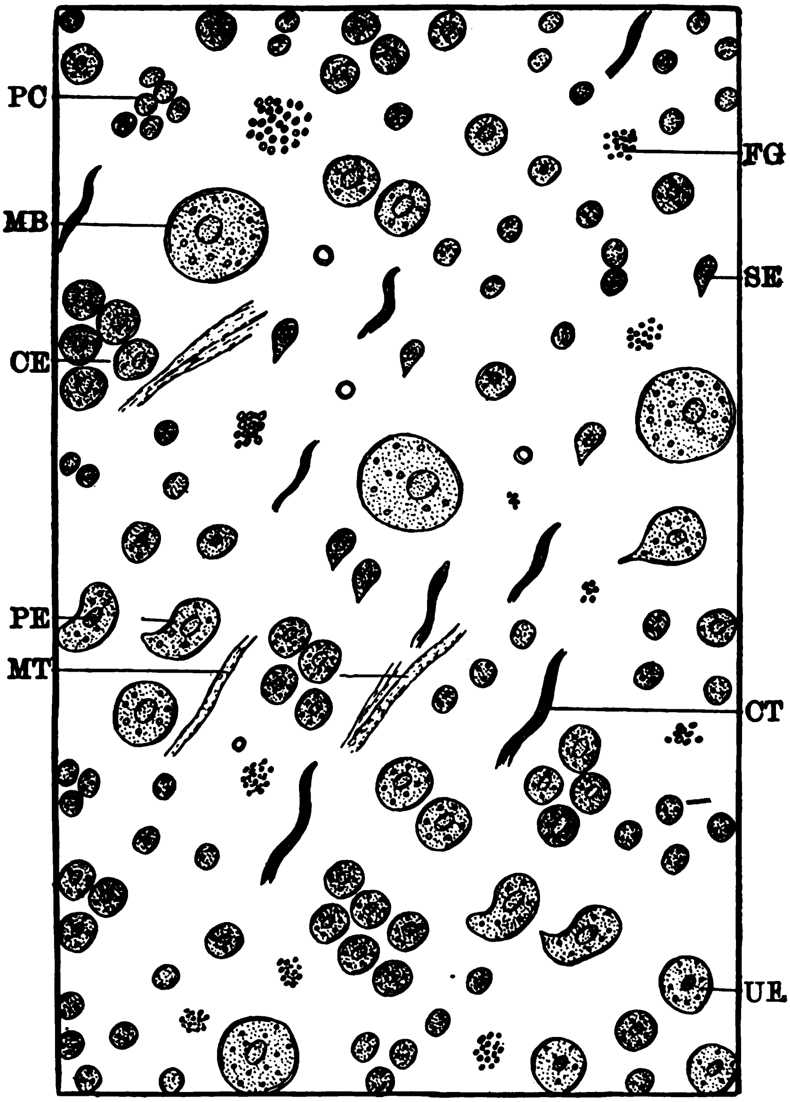

FIG. 104.—CIRRHOSIS OF THE KIDNEY, WITH CHRONIC CATARRHAL CYSTITIS (× 500).

PC, Pus-corpuscles; *CE*, epithelia from the convoluted tubules of the kidney, containing fat-globules; *SE*, epithelium from the straight collecting tubules of the kidney; *UE*, epithelium from the ureters; *PE*, epithelium from the pelvis of the kidney; *MB*, epithelium from the middle layers of the bladder; *CT*, connective-tissue shreds; *FG*, free fat-globules; *MT*, mucus-strings.

the acute eruptive and inflammatory diseases, especially scarlatina, diphtheria, and pneumonia; less frequently typhoid fever and smallpox. It is occasionally seen during pregnancy, though it is not always easy to account for its occurrence. Pressure produced by the gravid uterus may be partly responsible for it. In chronic affections, such as heart diseases, tuberculosis, and syphilis, it may also be seen, as well as in rarer cases of malarial poisoning.

As a result of strictures of the urethra, prostatitis, and hypertrophy of the prostate gland, parenchymatous nephritis is occasionally seen. The original inflammation is the cause of a cystitis, and, from the bladder, it ascends to the ureters, pelves, and kidneys, ending in a parenchymatous nephritis. A peculiar occurrence is its appearance in strong, healthy athletes during active training, especially when they subsist upon a meat diet; the same may be the case in fat people who desire to reduce their weight quickly by an exclusive meat diet.

Clinical Symptoms.—The clinical symptoms vary with the intensity of the process, though anæmia, headache, loss of appetite, emaciation, nausea, and loss of strength are all generally present. Severe acute cases may be ushered in by chills, followed by a rise in temperature. Very soon œdema will appear, first being localized, especially on the eyelids, but soon becoming general, involving the face, hands, feet, and cellular tissues generally. To these symptoms will be added dull, aching pains in the lumbar region, and, in the severe cases, uræmic symptoms.

Features Found in Urine.—Albumin is almost invariably present in comparatively large amount, and in some cases may be extremely abundant, reaching one-half of one per cent or even more. It is claimed that occasionally parenchymatous nephritis may exist without the presence of any albumin; that albumin may exceptionally occur in small quantities only is undoubted, but it is probably never absent altogether, as careful tests for albumin will show.

In acute parenchymatous nephritis the amount of urine is usually decreased, sometimes to a great degree, and in the severer and fatal cases may sink to a few ounces in the twenty-four hours, or may even be practically suppressed. The specific gravity in in many cases higher than normal, often reaching 1.030 or more, and the color dark, being sometimes quite pronounced, since hemorrhages frequently occur. The amount of solids, especially urea, voided during the twenty-four hours is usually decreased to a greater or less degree. In chronic nephritis the amount of urine is also at first decreased, but later becomes more abundant, though never in as pronounced a degree as in chronic interstitial inflammation. The specific gravity gradually becomes lower until in atrophy of the kidney it is never more than 1.012 or considerably less. The color varies, being pale in the later stages. The sediment found in the urine is always quite abundant, and when once separated does not readily mix with the watery portion.

As in interstitial nephritis, a positive diagnosis of croupous or parenchymatous nephritis is in many cases possible only from a microscopical examination of the urinary sediment. This will vary considerably in acute, subacute, and chronic cases. In this variety of nephritis the presence of casts in larger or smaller numbers is a constant feature, without which the diagnosis can never be made, and the greater the number of casts, the worse, as a rule, the inflammation. True casts will, however, never be found in urine without the presence at the same time of pus-corpuscles and kidney epithelia, the latter not only from the convoluted and narrow tubules, but frequently also from the straight collecting tubules, though these may be absent in mild cases.

The varieties and sizes of the casts are of great importance for the diagnosis and prognosis. In strictly acute cases we will never find fatty or waxy casts, and only occasionally a few granular casts, while hyaline and epithelial casts are always present in larger or smaller numbers, and blood casts in the severer, hemorrhagic forms. Again, the severity of the process can easily be determined by the size of the casts—when the smallest casts from the narrow tubules alone are present in small numbers, the parenchymatous nephritis will be of a mild character, and recovery is the rule. Casts from the convoluted and narrow tubules together, the former being of medium size, denote a process of moderate severity; but as soon as the largest casts, coming from the straight collecting tubules, are present with the other varieties, we know that the inflammatory process has affected the whole kidney—that is, both cortical and pyramidal substance —and is a severe one; therefore, a doubtful prognosis only can be given.

Acute Parenchymatous or Croupous Nephritis (Fig. 105).—When we examine the urine from a case of acute croupous nephritis, the features are found to be numerous and characteristic. The most pronounced elements are undoubtedly the casts, which are seen in varying numbers in every field of the microscope. In such cases, two varieties of casts are usually found—the hyaline and the epithelial, the latter studded with epithelia to a greater or less degree. The more numerous the casts, the severer the inflammation and the more albumin the urine usually contains.

Besides the casts, pus-corpuscles, red blood-corpuscles, and epithelia from the convoluted tubules are always present. They are found in moderate or large numbers, the kidney epithelia being frequently seen massed together. Red blood-corpuscles are found in every field, though, unless a hemorrhage has taken place, they cannot be called very abundant.

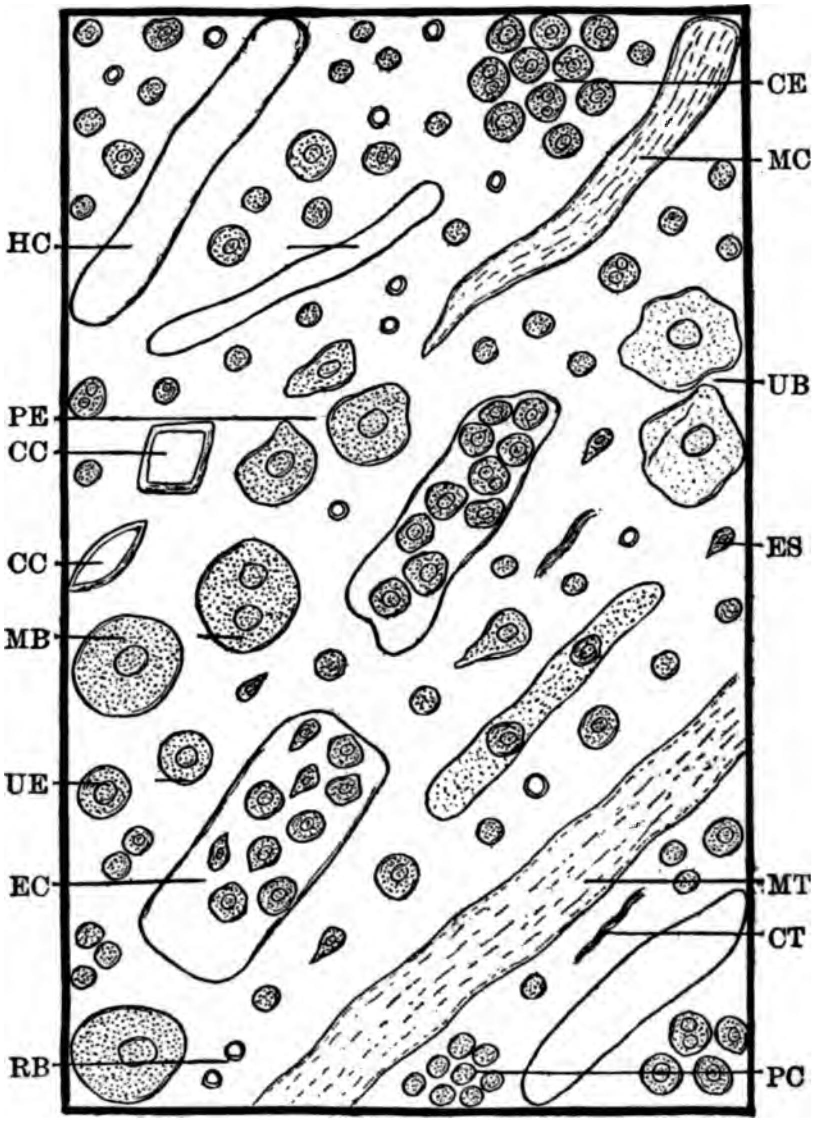

FIG. 105.—ACUTE PARENCHYMATOUS OR CROUPOUS NEPHRITIS, WITH PYELITIS AND CATARRHAL CYSTITIS (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles; *CE*, epithelia from the convoluted tubules of the kidney; *ES*, epithelium from the straight collecting tubules of the kidney; *UE*, epithelia from the ureter; *PE*, epithelia from the pelvis of the kidney; *UB*, epithelia from the upper layers of the bladder; *MB*, epithelia from the middle layers of the bladder; *CC*, creatinin crystals; *HC*, hyaline casts; *EC*, epithelial cast; *MT*, mucus-thread; *MC*, mucus-cast; *CT*, connective-tissue shred.

Epithelia from the straight collecting tubules may also be seen, and those from the ureter and pelvis of the kidney almost invariably accompany the other features. In some cases, there will also be an accompanying acute cystitis, shown by the presence of epithelia from the upper and middle layers of the bladder.

In these acute cases, mucus is present in fairly large amount, the pale strings being sometimes of considerable size, irregular, and finely striated. Not infrequently mucus is found in the form of casts—the so-called cylindroids. The presence of these has no further significance than the presence of mucus in general, and they may be seen in inflammations of any one of the genito-urinary organs. When they exist in a characteristic form, they can hardly be mistaken, as they are always faintly striated; but not infrequently they are so faint that their striation becomes visible only upon sharp focusing, and caution is here necessary not to mistake them for hyaline casts, which is frequently done. In size and shape they may resemble hyaline casts, which latter, however, are never striated. When they assume an irregular, convoluted form their diagnosis is easy.

In the severer cases of acute parenchymatous nephritis small shreds of connective tissue will be present; they are never large or numerous, and their higher refraction and pronounced fibrillary structure are sufficient to differentiate them from mucus. Besides these features, crystals of creatinin may be present in intense cases in which uræmic convulsions not rarely develop. The illustration is taken from a case of severe nephritis, which developed in the third week of scarlet fever and caused the death of the patient. The urine contained large numbers of characteristic creatinin lozenges and plates.

Besides the cases just described, severe cases with pronounced hemorrhages are often seen, and will give somewhat different features (Fig. 106).

The urinary sediment contains a large number of red blood-corpuscles in every field, together with many blood casts. The blood casts are partly filled with red blood-corpuscles, which have retained their normal appearance, and partly with disintegrated blood-globules, in the form of irregular brown masses, giving to the whole cast a rust-brown appearance; blood casts assume this character when they have been retained in the tubules for some time. Sometimes the larger portion of the cast contains fully formed red blood-corpuscles, while the disintegration has commenced in a small portion. Besides these casts, hyaline and epithelial casts are found in large numbers, and in these cases we almost invariably find large casts from the straight collecting tubules.

Epithelia from the straight collecting tubules are usually quite abundant, and connective-tissue shreds are larger and more numerous than in the preceding. In an active hemorrhage such connective-tissue shreds are cast off in fair numbers and found in the urine. Sometimes masses of fibrin are also found. The other features are the same, there being in most cases an accompanying inflammation of the pelves, the ureters, and the bladder.

Subacute Parenchymatous Nephritis (Fig. 107).—After a croupous or parenchymatous nephritis has lasted for some time, the casts, or rather some of the casts, commence to change. Such a change is rarely noticed until four or six weeks after the commencement of the inflammation, but occasionally, especially in nephritis after scarlet fever in children, may take place in one or two weeks.

The first change will be seen in the epithelial casts, some of the epithelia breaking down into granules, giving us an epithelial-granular cast. Very soon, however, perfect granular casts, without any trace of epithelia, are also found in small or moderate numbers, and these, in exceptional cases in children, can be seen as early as one week after the inflammation has started, being then scanty.

The next change which takes place is the transition of the granules into glistening, refractive fat-granules and -globules, at first only two or three being noticeable in a granular cast, and later on a larger number. Traces of the original epithelia may still be seen in the cast, while the largest portion has become changed into granules, and some of the granules into fat-globules, and we now have epithelial-granular-fatty casts. When the inflammation has lasted for six weeks or two months, small groups of free fat-globules, at first scanty, are also found, and a few globules are seen in the epithelia.

The other features, usually present in moderate numbers only, are the same as in an acute parenchymatous nephritis, and connective-tissue shreds are scanty, unless the case is a severe one. Mucus-threads and -casts may at times be pronounced, and the accompanying inflammations, especially in the bladder, are well marked.

Chronic Parenchymatous Nephritis.—The longer a nephritis lasts, the more marked are the changes in the casts, and in strictly chronic cases neither hyaline nor epithelial casts are seen in the urine. The granular casts are the most abundant in the milder forms, though a few fatty casts or granular-fatty casts are also present. The groups of free fat-globules, as well as the fat-globules in the epithelia and pus-corpuscles become more numerous and more pronounced.

In almost all cases of chronic croupous or parenchymatous nephritis, which have lasted for many months, and instead of abating have become more pronounced, a *fatty degeneration of the kidney* will develop, and we now have the so-called *large white kidney* (Fig. 108).

In these cases the fatty casts are abundant, and the large casts from

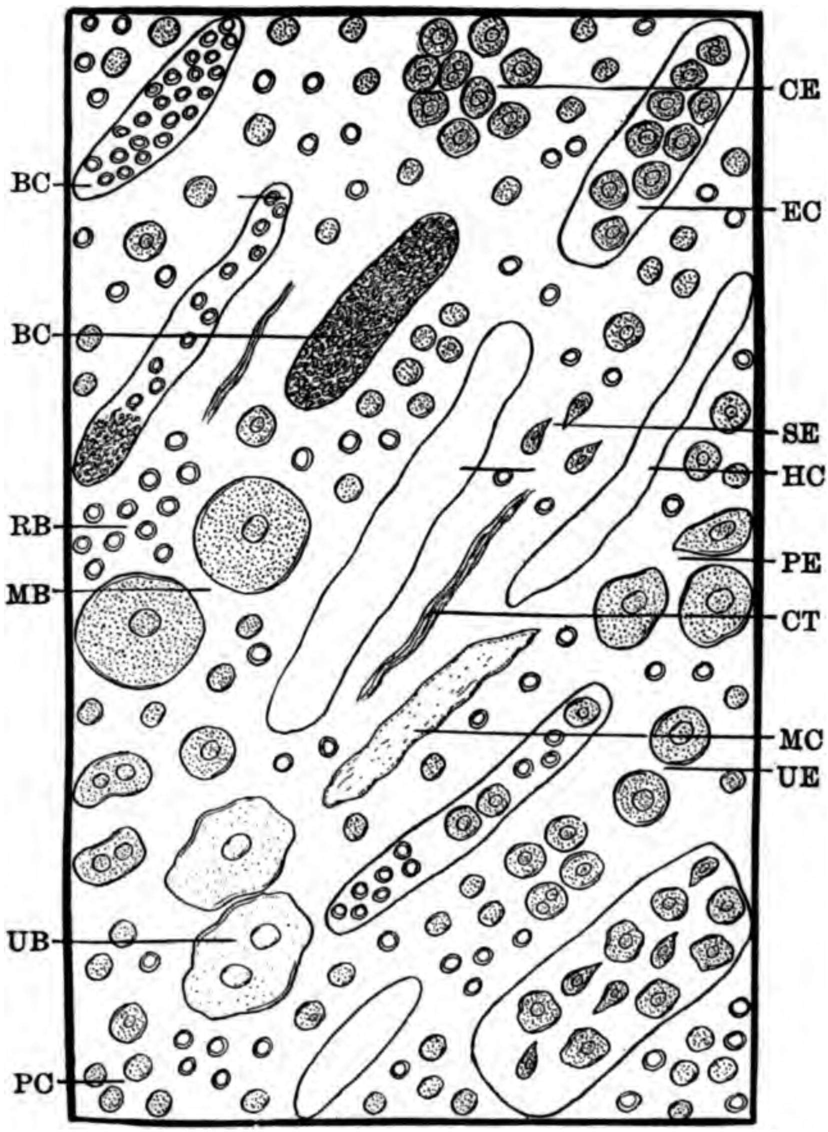

FIG. 106.—ACUTE HEMORRHAGIC PARENCHYMATOUS OR CROUPOUS NEPHRITIS, WITH PYELITIS AND CATARRHAL CYSTITIS (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles, *CE*, epithelia from the convoluted tubules of the kidney; *SE*, epithelia from the straight collecting tubules of the kidney; *UE*, epithelia from the ureter; *PE*, epithelia from the pelvis of the kidney; *UB*, epithelia from the upper layers of the bladder; *MB*, epithelia from the middle layers of the bladder; *HC*, hyaline casts; *EC*, epithelial cast; *BC*, blood casts; *CT*, connective-tissue shred; *MC*, mucus-cast.

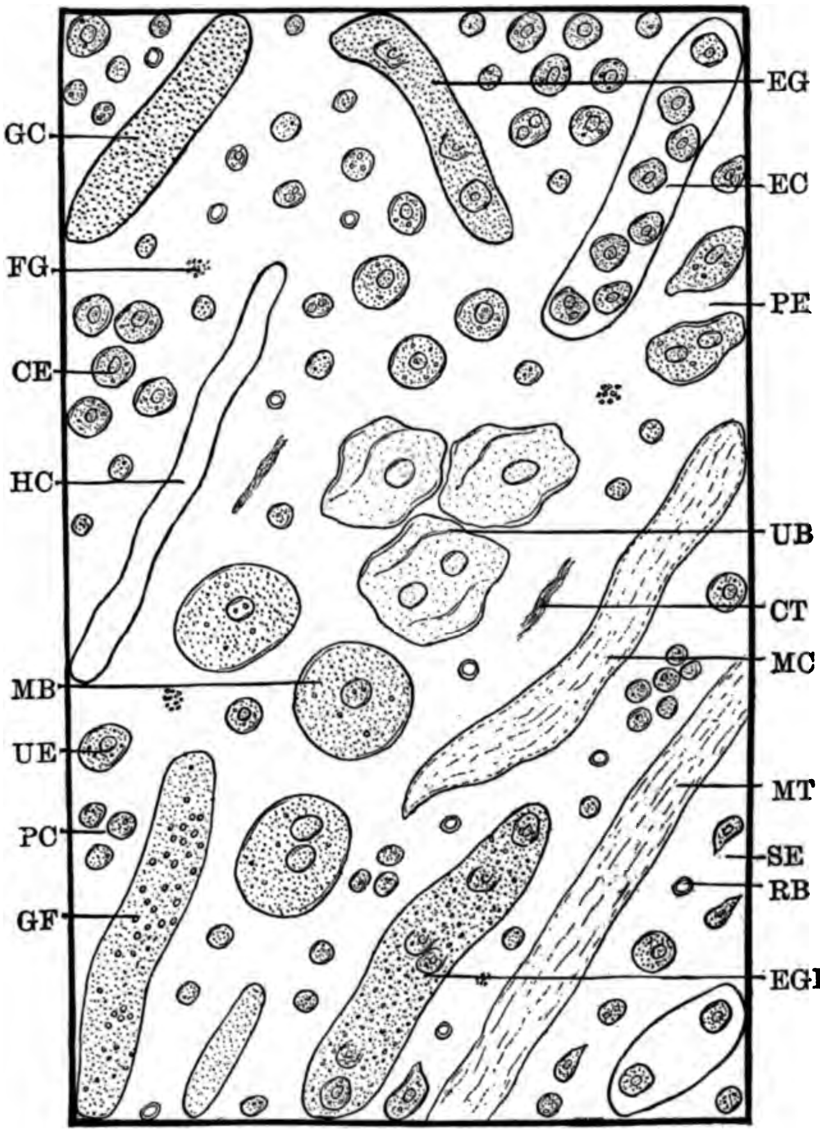

FIG. 107.—SUBACUTE PARENCHYMATOUS OR CROUPOUS NEPHRITIS, WITH PYELITIS AND CATARRHAL CYSTITIS (× 500).

RB, Red blood-corpuscle; *PC*, pus-corpuscles; *CE*, epithelia from the convoluted tubules of the kidney; *SE*, epithelium from the straight collecting tubules of the kidney; *UE*, epithelia from the ureters; *PE*, epithelium from the pelvis of the kidney; *UB*, epithelia from the upper layers of the bladder; *MB*, epithelia from the middle layers of the bladder; *HC*, hyaline cast; *EC*, epithelial cast; *GC*, granular-cast; *GF*, granular-fatty cast; *EGF*, epithelial-granular-fatty cast; *MT*, mucus-thread; *MC*, mucus-cast; *CT*, connective-tissue shred; *FG*, free fat-globules.

the straight collecting tubules are frequently seen in conjunction with the smaller casts. The fatty changes in the pus-corpuscles and epithelia are well marked, and the groups of free fat-globules and -granules are large and numerous. Here, too, individual fat-globules, much larger than those ordinarily seen, and sometimes attaining three or four times their size or even more, may be present. In rare cases needles of margaric acid in small numbers are found, but these are exceptional. Red blood-corpuscles are scanty in the majority of these cases.

Connective-tissue shreds are usually present, but, as a rule, are small and not numerous. The evidences of chronicity, as shown by the fat-globules, will be seen in all epithelia found in the urine; that is, both those from the convoluted and straight collecting tubules of the kidney, from the pelvis, the ureters, and the bladder. The epithelia from the straight collecting tubules are sometimes numerous, and may be just as abundant as the cuboidal epithelia. Pelvic epithelia are rarely absent, and those from the ureters are well marked. That a cystitis of varying degrees of intensity is always present need hardly be mentioned.

Besides the fatty degeneration, a *waxy or amyloid degeneration of the kidney* is found in a number of cases. Some authors call this an amyloid disease of the kidney, and claim that it is an independent affection and not associated with a parenchymatous nephritis. This view is undoubtedly incorrect, as a waxy degeneration of the kidney is usually a secondary affection found in chronic cases of nephritis. The exact cause and nature of such a degeneration are not known, and it is mostly found in chronic diseases, such as syphilis, tuberculosis, suppurative processes, ulcerations, and necroses. It seems to be due to some chemical change in the plasma of the blood, though the nature of this change is unknown.

Waxy degeneration of the kidney may occur in both interstitial and parenchymatous nephritis; it is much more common in the latter, and is rare in the former. It invades the epithelia of the uriniferous tubules, and ultimately produces waxy casts. Epithelia which have become waxy are highly glistening, and are found in the urine as more or less shining, homogeneous bodies. Not only the epithelia, but also the connective tissue, and simultaneously the walls of the blood-vessels, may undergo waxy degeneration.

The appearance of the urine is not characteristic of this degeneration, and it will present the features of a chronic nephritis, though the amount of sediment greatly varies, being sometimes slight, sometimes abundant. The specific gravity is usually low, and the amount of urine voided above normal. The diagnosis should never be made unless the changes in the urinary features are pronounced, and care must be taken not to mistake hyaline casts, which may in rare cases be somewhat glistening, for waxy casts.

In chronic parenchymatous nephritis with waxy degeneration of the kidney, the most characteristic features are the waxy casts (Fig. 109).

Waxy casts may occur in all sizes, are always of a high refraction, have wavy, convoluted contours, and frequently a yellowish color. The casts may assume different forms, and not rarely are so tortuous as to be likened to a corkscrew. In most cases all the three sizes of waxy casts will be found, and they may sometimes be mixed with other elements, such as granules—the granular-waxy; or with fat-globules—the fatty-waxy casts. The other features are the same as those in any chronic croupous nephritis. Pus-corpuscles are always present, as well as different epithelia, connective-tissue shreds in large numbers, and granular as well as fatty casts. The appearance of a waxy degeneration is usually of grave import, though even here recoveries have occurred, especially in children.

Cystic degeneration, which is also a secondary change, found in chronic cases of nephritis, does not give any characteristic symptoms in the urine, and, therefore, cannot be diagnosed as such.

Atrophy of the Kidney.—The result of a chronic croupous or parenchymatous nephritis is invariably atrophy of the kidney. The features of atrophy, as found in the urine, are characteristic, and a positive diagnosis can always be made, though the amount of urine voided in the twenty-four hours varies, is never as abundant as in cirrhosis of the kidney, and is usually considerably below the normal amount. The features are the following:

1. A continuously low specific gravity, as a rule never above 1.010, and occasionally not more than 1.006 or 1.004 at any time.

2. The presence of a large amount of albumin, in contradistinction to the small amount found in cirrhosis.

3. A considerable diminution of all salts.

4. Pus-corpuscles, present in moderate numbers, many, if not all, containing fat-granules and -globules.

5. Epithelia from the convoluted and straight collecting tubules of the kidney, in moderate numbers, many or all containing fat-granules and -globules.

6. Free fat-granules and -globules, sometimes in large numbers.

7. Granular, fatty, and in some cases even waxy casts in varying numbers, the former being usually quite abundant.

8. Connective-tissue shreds of moderate or large size, and always in at least fair numbers.

9. Red blood-corpuscles in varying numbers; these are practi-

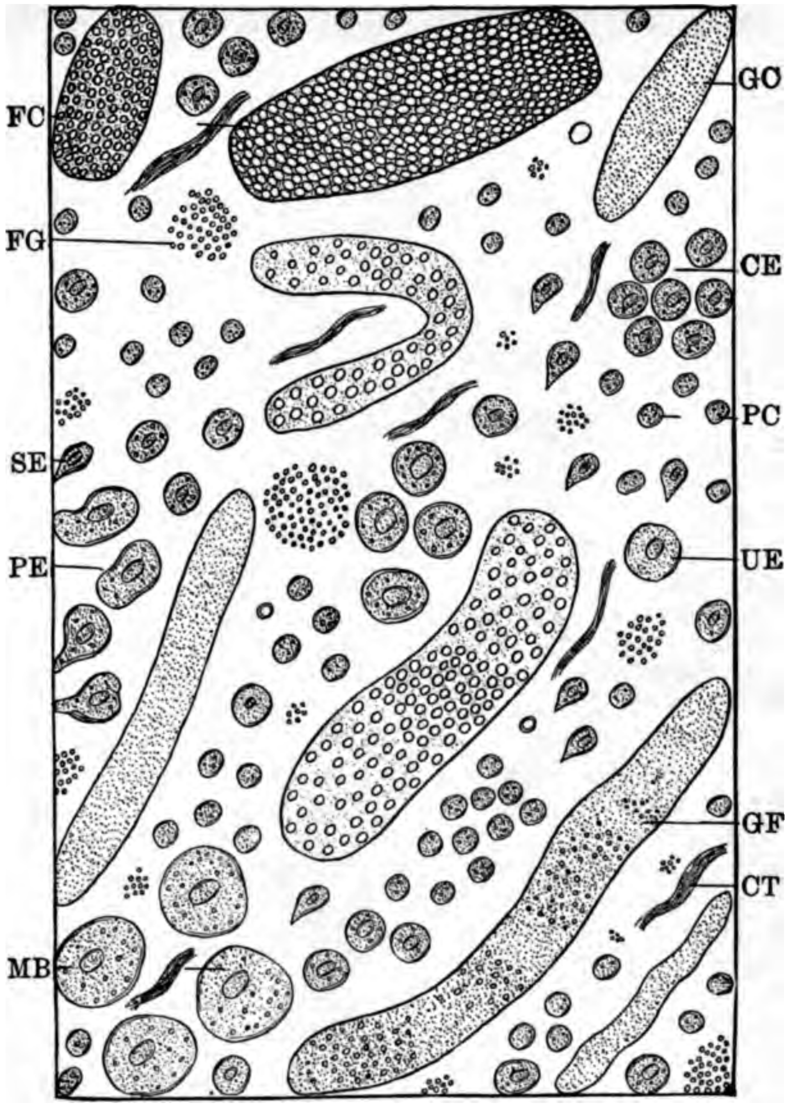

Fig. 108.—Chronic Parenchymatous or Croupous Nephritis with Fatty Degeneration of the Kidney, Accompanying Pyelitis and Catarrhal Cystitis (× 500).

PC, Pus-corpuscles; *CE*, epithelia from the convoluted tubules of the kidney; *SE*, epithelia from the straight collecting tubules of the kidney; *UE*, epithelium from the ureter; *PE*, epithelia from the pelvis of the kidney; *MB*, epithelia from the middle layers of the bladder; *GC*, granular cast; *FC*, fatty casts; *GF*, granular-fatty casts; *CT*, connective-tissue shreds; *FG*, free fat-globules.

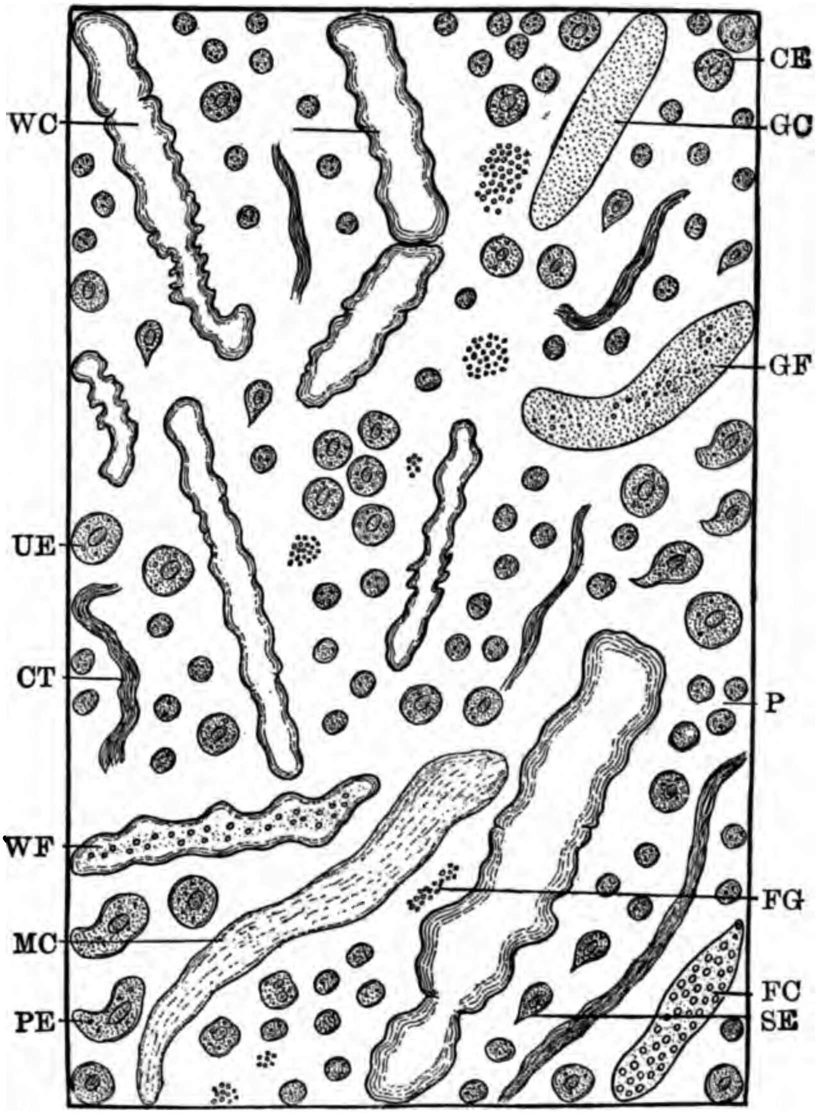

Fig. 109.—Chronic Parenchymatous or Croupous Nephritis, with Fatty and Waxy Degeneration of the Kidney, Accompanying Pyelitis (× 500).

P, Pus-corpuscles; *CE*, epithelia from the convoluted tubules of the kidney; *SE*, epithelia from the straight collecting tubules of the kidney; *UE*, epithelia from the ureter; *PE*, epithelia from the pelvis of the kidney; *GC*, granular cast; *GF*, granular-fatty cast; *FC*, fatty cast; *WC*, waxy cast; *WF*, waxy-fatty cast; *MC*, mucus-cast; *CT*, connective-tissue shred; *FG*, free fat-globules.

cally never absent, though they usually are scanty.

Epithelia from the pelvis of the kidneys, the ureters, and the middle layers of the bladder will be present in variable numbers.

Here, again, attention must be called to the fact that a badly diseased kidney, as an atrophied kidney always is, can never void many salts. In those cases in which the specific gravity is higher, and uric-acid, calcium-oxalate, or phosphate crystals are seen under the microscope, though all the other features admit of a positive diagnosis of atrophy of the kidney, we can reach the conclusion that only one kidney is as yet severely affected, since the salts must be voided by the other kidney. While a nephritis is in the greatest number of cases bilateral, both kidneys being affected, it occasionally happens that one kidney is less severely affected than the other. For a variable length of time the second kidney may remain functionally fairly efficient. The prognosis in all such cases is considerably better than when no salts whatever are seen.

Chronic Parenchymatous Nephritis, with Acute Parenchymatous Exacerbation.—In many cases of chronic parenchymatous nephritis, acute exacerbations may occur at any time, and fresh portions of the kidney tissue become inflamed. Such acute exacerbations can, in some individuals, be produced upon the slightest cause, as exposure to cold or errors in diet. It is not uncommon for an exacerbation of this kind to be produced every few weeks or months, leaving the patient weaker every time, and finally resulting in death.

A case of this kind, in which an acute croupous hemorrhagic exacerbation took place in a young man of twenty years, is shown in Fig. 110.

In this case, which ended fatally, all six varieties of casts, and of all three sizes, were present in large numbers. Not only were the regular casts seen, but a number of different combinations. The casts present were hyaline, epithelial, blood, granular, fatty, waxy, granular-fatty, epithelial-waxy, blood-waxy, and fatty-waxy.

Red blood-corpuscles were present in every field in moderately large numbers, and variously sized groups of fat-globules were also abundant. Pus-corpuscles were numerous, and epithelia from the convoluted as well as the straight collecting tubules of the kidney were present in large numbers, many studded with fat-globules. Connective-tissue shreds were present, and mucus in the form of threads, and especially casts, could be seen in many fields. Of the accompanying inflammations, the pyelitis was the most severe, though the inflammations of the ureters and bladder were well marked.

Salts were entirely absent under the microscope and the specific gravity was low. The diagnosis that probably both kidneys were affected in a severe degree was made, and a bad prognosis had to be given. The patient died within two weeks after the examination.

From the descriptions here given, it will be seen that the varieties of casts found in parenchymatous or croupous inflammations of the kidney tend to show whether the process is acute, subacute, or chronic. When hyaline, epithelial, or blood casts are found in a case giving all the symptoms of chronicity, we can be certain either that an acute exacerbation has taken place in the same kidney or that the second kidney has become acutely inflamed. Sometimes cases of a so-called acute inflammation show granular and even fatty casts in large numbers, but careful questioning of the patient will bring out the fact that he has not been perfectly healthy for a long time, though he may have been able to attend to his business in spite of headache and general malaise. The only cases in which purely granular casts in small numbers may occasionally be seen one or two weeks after the commencement of the inflammation, are those already mentioned, especially in children after scarlet fever. Waxy casts never appear in acute inflammations, but always denote chronicity.

SUPPURATIVE NEPHRITIS.

Suppurative nephritis, also called abscess of the kidney, or surgical kidney, the most intense of the three primary varieties of nephritis, is an independent process, and must not be confounded with acute interstitial nephritis or non-suppurative pyelo-nephritis. There may be either a number of small, disseminated foci of suppuration, or one large abscess, usually confined to one kidney. Sometimes the suppuration may be so excessive that the larger part of the structure of the kidney has disappeared, and a large, thick-walled cavity filled with pus is found in its place; these cases are spoken of as pyonephrosis.

Causes.—The causes of a suppurative nephritis are not always plain, though in many cases the disease is the result of an extension of the inflammatory process from some other portion of the genito-urinary tract. A simple gonorrhœa, which gradually extends upward, may be sufficient to cause it, and both urethral strictures and inflammation and hypertrophy of the prostate gland may be causes. The use of unclean sounds and catheters, even in these days of antisepsis, is not rarely followed by an abscess of the kidney.

Occasionally the disease follows different acute infectious diseases, such as typhus and typhoid fevers, cholera, and diphtheria, or may be seen with pyæmia and carbuncles. In renal tuberculosis abscesses are quite common, and they may also occur when calculi are present. In

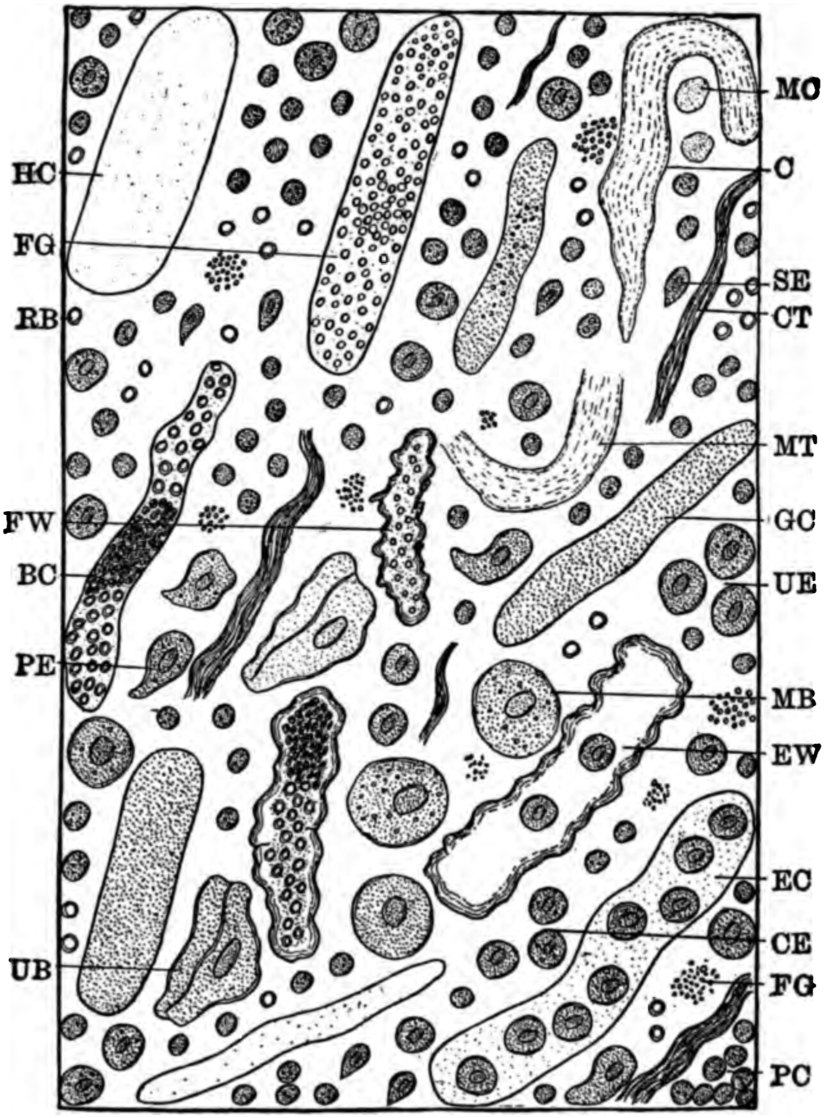

FIG. 110.—CHRONIC PARENCHYMATOUS OR CROUPOUS NEPHRITIS, WITH FATTY AND WAXY DEGENERATION OF THE KIDNEY AND AN ACUTE HEMORRHAGIC CROUPOUS EXACERBATION, PYELITIS, AND CATARRHAL CYSTITIS (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles; *CE*, epithelia from the convoluted tubules of the kidney; *SE*, epithelia from the straight collecting tubules of the kidney; *UE*, epithelia from the ureter; *PE*, epithelia from the pelvis of the kidney; *UB*, epithelium from the upper layers of the bladder; *MB*, epithelium from the middle layers of the bladder; *HC*, hyaline cast; *EC*, epithelial cast; *BC*, blood-cast; *GC*, granular cast; *FC*, fatty cast; *FW*, fatty-waxy cast; *EW*, epithelial-waxy cast; *CT*, connective-tissue shred; *MT*, mucus-thread; *MC*, mucus-corpuscle; *C*, mucus-cast; *FG*, free fat-globules.

still other cases the etiology remains obscure, and we can only surmise that pyogenic organisms in large numbers have settled in a perhaps previously inflamed kidney.

Clinical Symptoms.—Acute abscesses are usually ushered in by pronounced chills, followed by a rise in temperature and general depression. Pain, as a rule, is present, although it is not always referred to the seat of the abscess. Emaciation, nausea, and vomiting can occur. After an abscess has ruptured, it may continue to discharge pus for a long time, becoming chronic. In these cases the acute symptoms gradually subside, though a slight fever is always present, and pain or tenderness either in the region of the kidney or in the inguinal region, testicles, or legs is a constant feature.

Features Found in Urine.—The urine in suppurative nephritis is always cloudy, and a pronounced heavy sediment invariably forms. The specific gravity varies considerably, but is mostly below normal, and the amount of urine is diminished. Albumin is present in large amount in every case.

The clinical symptoms are at times so vague that a positive diagnosis is generally possible only through a microscopical examination of the urinary sediment. The features found under the microscope will at once clear up the diagnosis, and it does not seem necessary for the abscess to have ruptured; emigrated pus-corpuscles and the shedding of connective-tissue shreds are sufficient for a diagnosis as long as no firm membrane has formed around the abscess.

The microscopical features are the presence of a large number of pus-corpuscles, many kidney epithelia, usually from both the convoluted and straight collecting tubules, and a varying number of red blood-corpuscles, the latter being quite abundant in acute abscesses. Besides these, connective-tissue shreds are always found, in either moderate or large amount. Without such shreds, abscess of the kidney should never be diagnosed, since these alone show a destruction of the kidney tissue. Epithelia from the pelvis of the kidney almost invariably accompany the affection. Casts may be either present or absent; when present, they denote a complicating parenchymatous nephritis.

The features seen in a chronic suppurative nephritis are shown in Fig. 111.

The pus-corpuscles are extremely numerous, and may so entirely fill some fields that no other features become visible. In other fields, however, epithelia from the convoluted tubules of the kidney will be found in large numbers, and, as a rule, those from the straight collecting tubules are also present. Fat-globules and -granules are abundant, partly lying free in variously sized groups, partly filling the pus-corpuscles and epithelia to a greater or less degree. Connective-tissue shreds are present, being large and abundant.

Red blood-corpuscles are always found, but in such cases in small numbers only, while not infrequently rust-brown crystals of hæmatoidin, in the form of needles and plates, but especially the former, denoting a previous hemorrhage, are seen. These will be found in the pus-corpuscles and epithelia, as well as free. In the case depicted, the hæmatoidin crystals are very abundant, being found in the form of large conglomerations of irregular, curved needles and stars, as well as smaller plates. Epithelia from the pelvis of the kidney, the ureter, and the bladder, denoting an inflammation of these organs, are also fairly numerous. In addition, numerous bacteria are usually present.

Although these features are perfectly characteristic, we not infrequently find another, the so-called endogenous new-formation of pus-corpuscles in different kidney and even pelvic epithelia, denoting, if present in large numbers, a pressure. Such a diagnosis will, therefore, hardly ever present any difficulties, contrary to the opinion frequently held that it is impossible to diagnose an abscess from the examination of the urine alone.

Abscesses not directly in the kidney substance, but pressing upon the kidney—perirenal abscess—may also be diagnosed. These will show the same features in the urine, though perhaps somewhat less marked, together with endogenous new-formations in the kidney epithelia. Whenever these are seen in many epithelia, they are caused by long-continued pressure upon the kidney, and their presence justifies the diagnosis.

SUPPURATIVE PYELITIS.

An abscess may develop in the pelvis of the kidney instead of in the kidney proper. The causes of this are the same as for suppurative nephritis, though perhaps calculi will more frequently produce an abscess here than in the kidney proper. The symptoms do not differ from those of suppurative nephritis, and the exact location of the abscess can only be determined by microscopical examination of the urine (Fig. 112).

In an acute suppurative pyelitis, red blood-corpuscles are always present in moderate or even large numbers, and pus-corpuscles are extremely numerous. The diagnosis can be made from the cuboidal and irregular pelvic epithelia, which in these cases are abundant, and may be found in groups. In such abscesses epithelia from all the different layers of the pelvis will be present. These epithelia may vary considerably in size, and a few may be even as large as those from the middle layers of the bladder. There should, however, be no difficulty in diagnosing them, since these

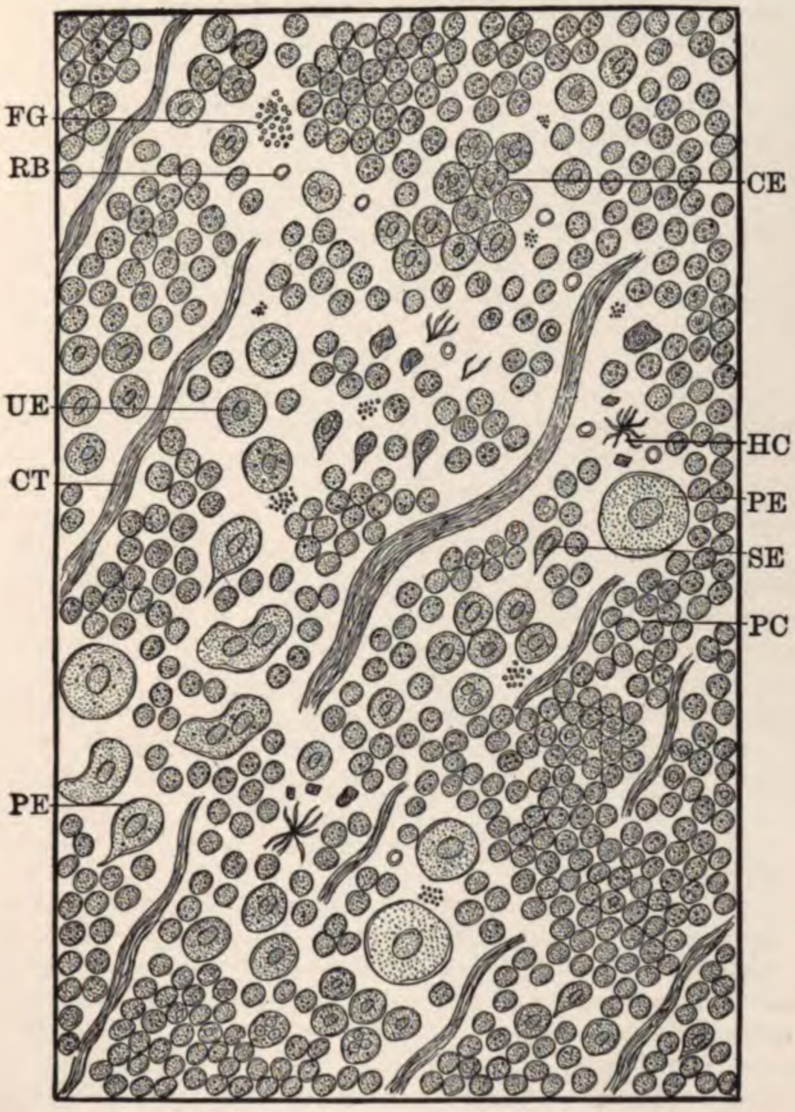

FIG. 111.—CHRONIC SUPPURATIVE NEPHRITIS, WITH CATARRHAL PYELITIS (× 500).

RB, Red blood-corpuscle; *PC*, pus-corpuscles; *CE*, epithelia from the convoluted tubules of the kidney; *SE*, epithelium from the straight collecting tubules of the kidney; *UE*, epithelia from the ureter; *PE*, epithelia from the pelvis of the kidney; *CT*, connective-tissue shreds; *HC*, hæmatoidin crystals; *FG*, free fat-globules.

large epithelia are irregular, angular, lenticular, or pear-shaped. Connective-tissue shreds are numerous, and without them no such diagnosis must be made.

In all cases epithelia from the ureter, showing a secondary inflammation, are quite abundant, and in many of them endogeneous new-formations of pus-corpuscles will be found. Epithelia from the convoluted tubules of the kidney need not necessarily be present in acute cases, but sooner or later a moderate number, the indication of an accompanying nephritis, are seen; here, too, endogenous new-formations can appear. Very soon a cystitis will develop, and the epithelia from the bladder accompany the other features.

In a chronic abscess of the pelvis the features are the same as those described in suppurative nephritis, except that the comparative number of the pelvic and kidney epithelia becomes changed, the former being considerably more numerous than the latter.

TUBERCULOSIS OF THE KIDNEY.

Although renal tuberculosis can undoubtedly exist as a primary disease, it is comparatively rare, being most frequently associated with tuberculosis in other organs. It may result from an extension of the tubercular process from other portions of the genito-urinary tract. In the kidney we will generally find evidences of a chronic interstitial or catarrhal nephritis, though in rare cases a parenchymatous or croupous inflammation accompanies the tubercular process. The tubercular nodules in different portions of the kidney enlarge, and, after a time, usually break down, so that ulcers or abscesses are formed.

Features Found in Urine.—The appearance of the urine is not characteristic in these cases; the color is usually pale, and it is turbid and of a low specific gravity. The amount of urine is increased, and a small amount, sometimes only a trace, of albumin is present. The sediment is slight, unless ulcers or abscesses have formed, when it is more profuse.

The features under the microscope are at first those described in a chronic interstitial nephritis, and later on give evidences of a destructive process, with the presence of connective-tissue shreds in varying amount. In most cases a pronounced cystitis is associated with the process, and not rarely ulcers will be formed in the bladder. Such a chronic ulcerative cystitis should always be looked upon with suspicion, as being possibly due to a tuberculosis.

Whenever tuberculosis is suspected in the kidneys, and the evidences of a chronic interstitial nephritis are found in the urine, examinations for tubercle bacilli must be made. This is not infrequently a tedious process, as the bacilli are rarely present in large numbers; yet the diagnosis cannot be made with certainty without them. Repeated examinations of many drops, from urine taken at different times of the day, will never fail to reveal them. In exceptional cases they are quite numerous.

It is of the utmost importance that a diagnosis of the presence of a renal tuberculosis be made as early as possible, the more so since, in contradistinction to nephritis generally, tuberculosis in many cases at first attacks one kidney only, and may remain confined to that kidney for a variable length of time. If the process continues, and the diseased kidney is not removed, an inflammation of the second kidney will surely set in, and impair its functional efficiency. Although renal tuberculosis is more frequently found in young individuals, it is occasionally seen in persons of middle age or beyond middle age.

In every case in which there is any suspicion of the presence of tuberculosis of the kidney, ureteral catheterization should be resorted to, and the urine from each kidney examined separately for the presence of tubercle bacilli. Examination of ureteral catheter urines is much more satisfactory, and tubercle bacilli are more readily found when present, than in a mixed bladder urine. When, in spite of a negative result, the symptoms persist, and urine examination distinctly shows an inflammatory condition of the kidney, guinea-pig inoculations should always be made. Often enough such inoculations alone will positively determine the presence or absence of a tuberculous process.

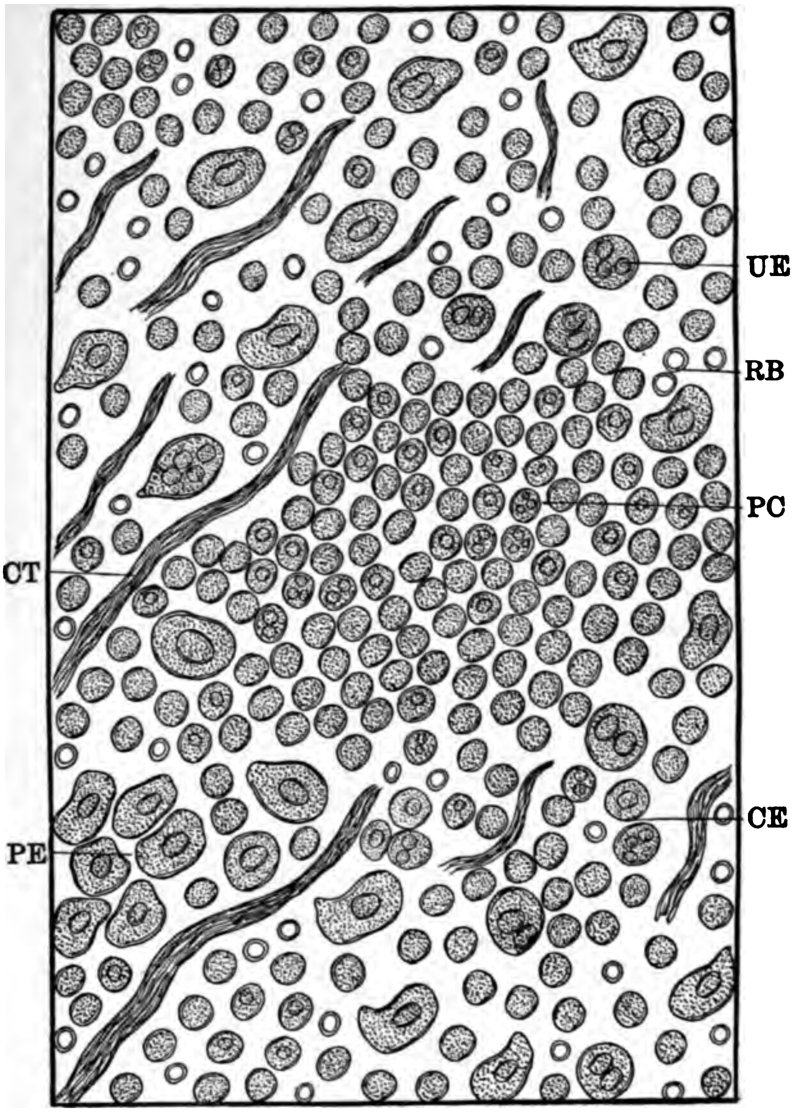

Fig. 112.—Acute Abscess of Pelvis of Kidney, or Acute Suppurative Pyelitis (× 500).

_RB_, Red blood-corpuscles; _PC_, pus-corpuscles; _UE_, epithelium from the ureter; _PE_, epithelia from the pelvis of the kidney; _CE_, epithelia from convoluted tubules of the kidney; _CT_, connective-tissue shreds.

II. *ANOMALIES OF SECRETION.*

Of great importance in the diagnosis of kidney lesions are the anomalies of secretion, under which term the conditions known as *lithæmia* and *oxaluria* are included. Sooner or later these will in many cases produce an inflammation of the kidney proper, as well as the pelvis of the kidney, and may in pronounced cases cause hemorrhages from the kidney and pelvis, as well as abscesses.

Both lithæmia and oxaluria are of frequent occurrence, and need not of necessity lead to the production of calculi, though this may occur. Persons so affected will pass large quantities of uric acid or calcium oxalate, or both, and their urine almost invariably has a high specific gravity.

Causes.—The causes of these conditions are practically unknown. It was believed that persons who live high, eat an excessive amount of meat as well as starchy and saccharine substances, and drink considerable champagne are predisposed to the so-called uric-acid diathesis. This is undoubtedly true in some cases; but in others just the opposite conditions prevail, and still uric acid is voided in large amounts.

Clinical Symptoms.—The clinical symptoms in these cases, which are much the same in both conditions, are headache, general malaise, dyspepsia, irregularity of the bowels, sleeplessness, neurasthenia, and later on melancholia. Frequent urination with a burning sensation in the urethra may be present, and there is often a dull, aching feeling in the lumbar region. In lithæmia fleeting pains in legs, knees, hands, and arms may also exist. Persons so affected are always irritable, and sooner or later suffer from neurasthenia and melancholia; they may be treated for a variety of affections before the true cause of their condition is discovered.

LITHÆMIA.

The microscopical features in the urinary sediment of a person affected with lithæmia are quite characteristic (Fig. 113).

Crystals of uric acid are found in large numbers, and as a rule different varieties, such as the common form, that seen in highly acid urine, and irregular plates and needles, are present. The crystals may attain large sizes, but usually the smaller sizes only are met with. Besides these, crystals of calcium oxalate in moderate numbers are also present. In many cases which come under observation pus-corpuscles are found in small or moderate numbers, as well as different epithelia, more especially those from the pelvis of the kidney and the ureters, though epithelia from the convoluted tubules in small numbers and bladder epithelia are rarely absent. Red blood-corpuscles are not numerous when no hemorrhage has taken place, though a few are always seen. A few fat-globules are usually seen in the pus-corpuscles and epithelia.

In these, the common cases of lithæmia, we have, therefore, an inflammation of moderate severity only, either a simple pyelitis or a pyelonephritis, with an accompanying cystitis. The inflammation, when seen, is rarely acute, but usually subacute or chronic. Such a condition may go on for many years without producing any other features.

When large numbers of these salts are continually produced and deposited in the pelves and calices of the kidneys, smaller or larger concretions or calculi will then be formed, and cause more pronounced symptoms. In such cases the first symptom is not infrequently a hemorrhage from the kidney or pelvis, with more or less severe pain. All the features of such a hemorrhage, together with concretions of uric acid, will be found in the urine. After a day or two the symptoms may subside, but, if the causes leading to the formation of the salts still continue, will recur sooner or later.

Hemorrhage from the Pelvis of the Kidney.—Hemorrhage from the pelvis of the kidney, due to uric-acid calculus, gives characteristic features in the urine, from which the diagnosis can easily be made (Fig. 114).

The field is crowded with red blood-corpuscles, which vary very considerably in shape, size, and appearance. As the urine is usually not examined until a number of hours after it is voided, comparatively small numbers will be found containing hæmoglobin, and they are therefore of a yellowish or slightly brown color. The larger numbers usually have lost the hæmoglobin, and these corpuscles will appear colorless, with a distinct double contour. They are found either singly or conglomerated in large groups. Crenated red blood-corpuscles are frequently found, but in small numbers only, and they may also be seen edgewise. When they have imbibed water, they swell, and may be even double their usual size. Again, a varying number of hæmatoblasts, which present the features of red blood-corpuscles, but are only half their size, are often seen in an active hemorrhage. White blood-corpuscles, which may be twice the size of the fully formed red blood-globules, and cannot be distinguished from pus-corpuscles, are present in small numbers. They are always granular, either pale with a fine granulation or more glistening and having a coarser granulation. When comparatively few of these corpuscles are seen, we know that they are not pus-corpuscles, and their presence should never cause the diagnosis of an inflammation.

Besides the blood-corpuscles, uric-acid crystals, in the form of irregular plates, masses, and needles, are abundant. They vary considerably in size, are always colored, and may be either single or conglomerated.

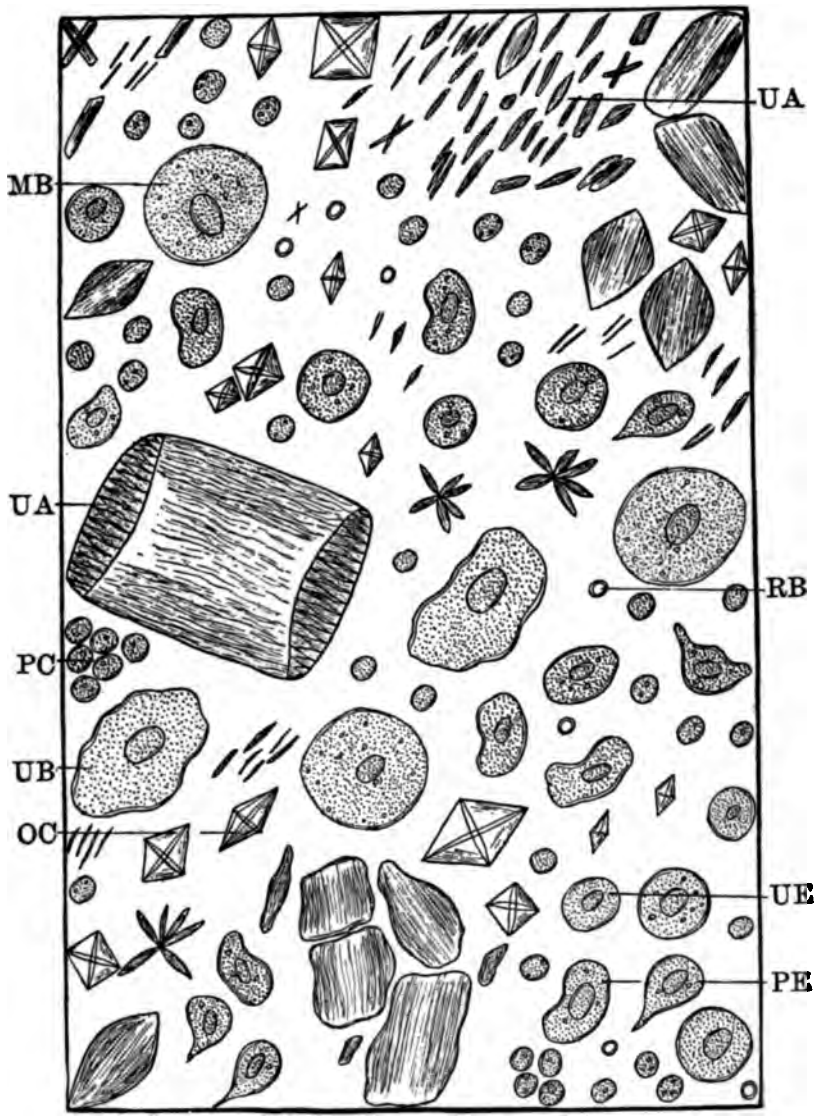

Fig. 113.—Lithæmia, with Subacute Pyelitis and Catarrhal Cystitis (× 500).
UA, Uric-acid crystals; *OC*, calcium-oxalate crystals; *RB*, red blood-corpuscle; *PC*, pus-corpuscles; *PE*, epithelia from the pelvis of the kidney; *UE*, epithelium from the ureter; *UB*, epithelium from the upper layers of the bladder; *MB*, epithelium from the middle layers of the bladder.

The needles may be seen in groups containing individual small formations, which sometimes appear like small granules, or they are large and form stellate masses. These are the forms which, when small, produce gravel; when large, are portions of calculi, and may lodge in the pelvis of the kidney.

Epithelia from the pelvis of the kidney, varying in size but always characteristic, are more or less numerous. When the hemorrhage is severe, many fields may sometimes have to be examined before they are discovered, and the place of origin of the hemorrhage becomes clear; but they are always present, often in groups of three, four, or more. Smaller epithelia from the ureter are also seen. Connective-tissue shreds are never absent, though their number and size may be small. In pronounced cases they are usually found in large numbers.

Besides these features, variously sized masses of fibrin, in the form of thin, pale, often colorless strings, consisting of wavy bands, may sometimes be seen, and irregular clots of blood can also be found. In such hemorrhages all the features, including the epithelia and connective-tissue shreds, may occasionally have a yellowish color from the hæmoglobin; but this is not the rule, unless the centrifuge has been used and the examination made immediately after the urine is passed.

Pyelitis Calculosa.—In the so-called pyelitis calculosa, an inflammation or even suppuration of the pelvis is present, and due to calculi, the most common of which are uric acid and calcium oxalate, though phosphatic stones are also not rare. The features are the same as those found in any catarrhal or suppurative pyelitis, with the addition of concretions. Red blood-corpuscles are invariably present in such cases, but, unless a hemorrhage occurs in the course of the inflammation, never in large numbers.

OXALURIA.

Among the anomalies of secretion, oxaluria plays an important part. It is far more common than is generally supposed, and in all cases giving vague neurasthenic symptoms the urine should be examined. The specific gravity is usually high, varying between 1022 and 1030 or higher, and the amount of urine passed may be considerably below the normal. The microscope always shows large numbers of crystals of calcium oxalate, in all shapes and sizes, and even in the milder cases an irritation of the pelvis of the kidney is rarely absent, so that a small number of pus-corpuscles and pelvic epithelia is found. Instead of an irritation, all the grades of inflammation may at different times exist, though oxaluria alone, without the presence of a stone, does not cause suppuration.

When many crystals are present, minute concretions, which are so small as to give no special symptoms, are frequently passed, and these, in a few cases, may cause hemorrhages from the pelvis. In a number of cases which have come under observation, prolonged hæmaturia existed, but the cause could not be discovered, as there was no pain connected with it and no symptom to suspect the presence of a calculus. Microscopical examination showed those minute concretions, and easily cleared up the case.

HÆMOGLOBINURIA.

Hæmoglobinuria is a rare condition, which is characterized by a dissolution of the red blood-corpuscles and the appearance in the urine of the coloring matters of the blood in solution. The red color of the urine which is always found in these cases is, therefore, not due to the presence of a large number of red blood-corpuscles, as in hæmaturia, but to that of dissolved hæmoglobin.

Causes.—The affection is occasionally seen after poisoning with different substances, such as carbolic acid, sulphuric acid, naphthol, muriatic acid, pyrogallic acid, and even chlorate of potash. It may occur in the course of severe infectious and contagious diseases, such as hemorrhagic variola, malignant scarlatina, and yellow fever, as well as in intense malaria. After extensive burns, in scurvy, and purpura it has also been described.

Besides these, it may occur as an idiopathic disease of intermittent character—the paroxysmal hæmoglobinuria—which is said to develop sometimes in rare cases of syphilis. In such cases urine containing hæmoglobin may be voided either for a few hours only, or more rarely for days or even weeks, accompanying symptoms much like those of intermittent fever. As a rule, attacks of this kind follow exposure to cold.

Features Found in Urine.—The appearance of the urine in hæmoglobinuria is always dark red or brownish, the sediment being abundant. The specific gravity varies considerably, but, as a rule, is slightly increased. Albumin will be found in varying amount. Although the disease is by no means a distinct kidney affection, changes having taken place in the blood, a nephritis of varying degrees of intensity usually accompanies it, and its features are found in the urine.

The microscopical elements in a pronounced case of hæmoglobinuria, which occurred in yellow fever, are illustrated in Fig. 115.

The urinary sediment contains an extremely large number of dark or rather rust-brown masses, made up of granular matter, as well as granules scattered irregularly over the field. The masses vary considerably in size, some being small, but others large, and may assume different shapes; these are the masses and granules of hæmoglobin.

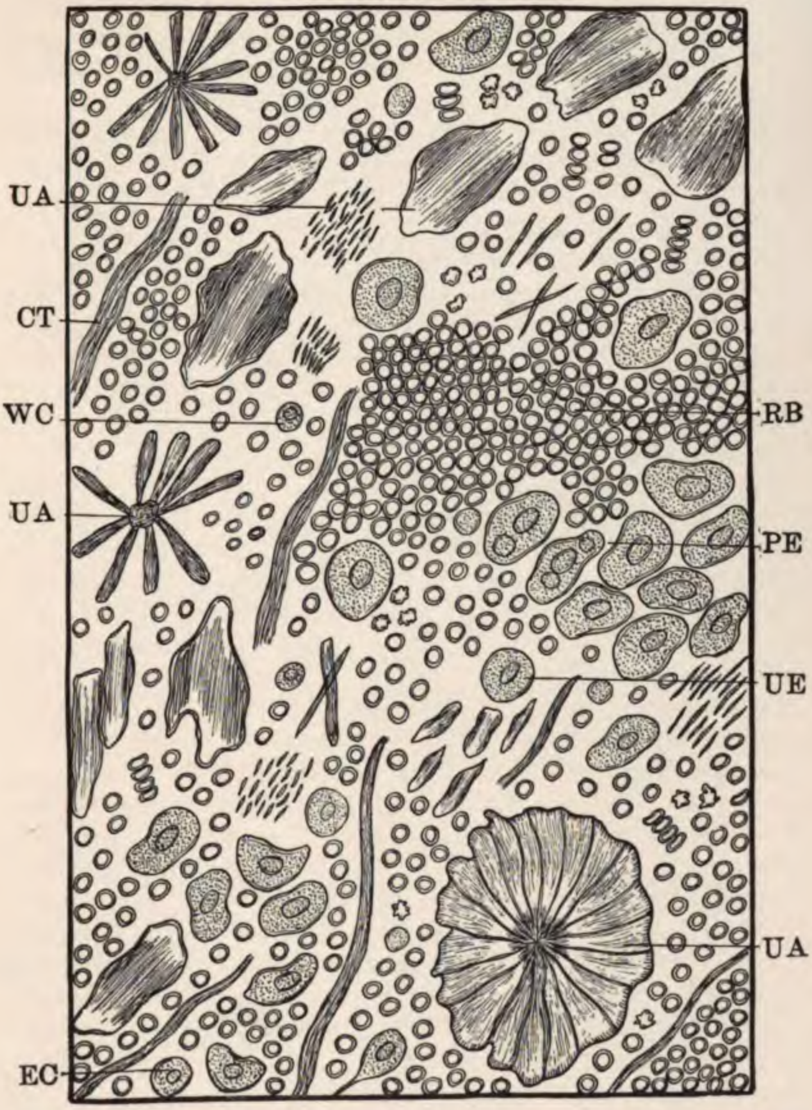

Fig. 114.—Hemorrhage from Pelvis of Kidney, Due to Uric-Acid Calculus (× 500).

UA, Uric-acid crystals; *RB*, red blood-corpuscles; *WC*, white blood-corpuscle; *PE*, epithelia from the pelvis of the kidney; *UE*, epithelium from the ureter; *EC*, epithelium from the convoluted tubules of the kidney; *CT*, connective-tissue shreds.

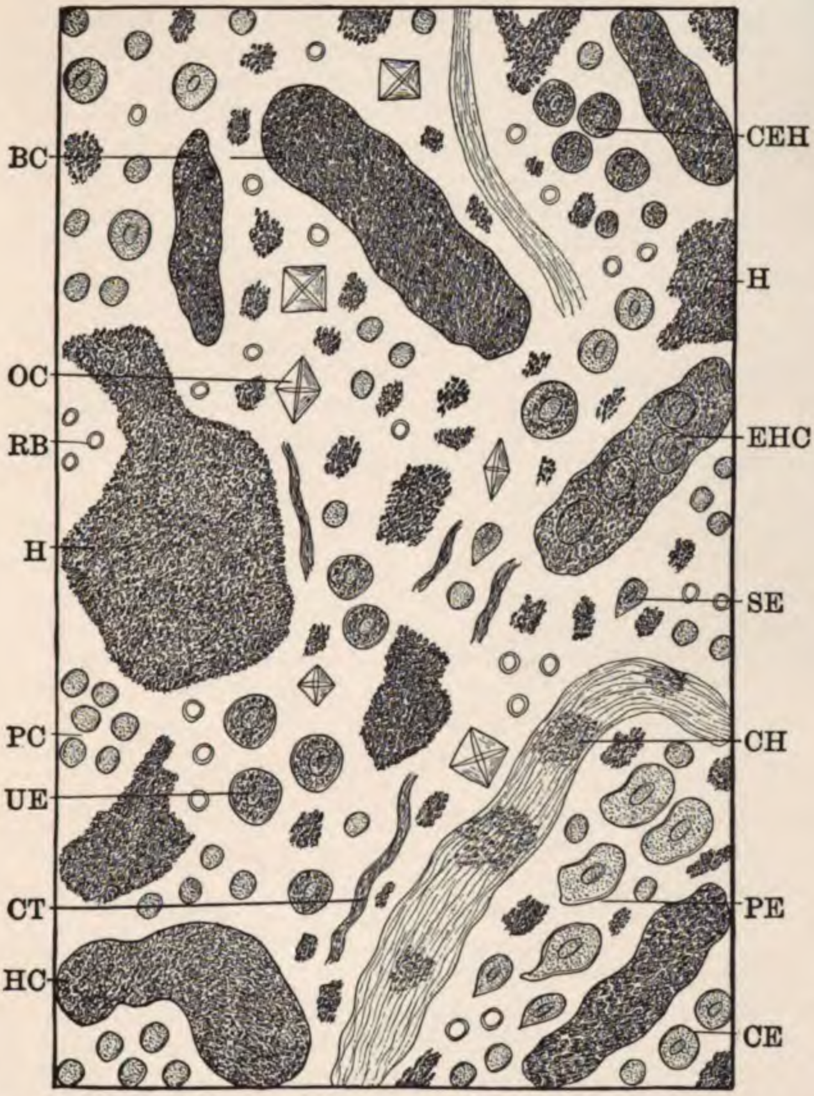

FIG. 115.—HÆMOGLOBINURIA, ACUTE HEMORRHAGIC CROUPOUS OR PARENCHYMATOUS NEPHRITIS, WITH CATARRHAL PYELITIS (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles; *H*, hæmoglobin; *CE*, epithelia from the convoluted tubules of the kidney; *SE*, epithelium from the straight collecting tubules of the kidney; *CEH*, epithelia from the convoluted tubules, filled with hæmoglobin; *PE*, epithelia from the pelvis of the kidney; *UE*, epithelia from the ureter; *HC*, hæmoglobin cast; *BC*, blood cast; *EHC*, epithelial cast filled with hæmoglobin; *CT*, connective-tissue shred; *CH*, cylindroid with hæmoglobin; *OC*, calcium oxalate crystals.

Hæmoglobin is also found in the form of casts, which appear filled with dark brown granules, but differ from blood casts by their greater irregularity. The latter are rarely absent, though the blood-corpuscles are never found fully formed in the casts, but always disintegrated, and of a rust-brown color. Epithelial casts are frequently present and are also studded with hæmoglobin.

Red blood-corpuscles are never entirely absent in these cases, though they are comparatively scanty, and always, even in the freshly voided urine, appear very pale and double contoured, having completely lost their coloring matter.

Besides these features, pus-corpuscles and epithelia are present, many of which are entirely filled with granules of hæmoglobin and have a dark brown color. Pus-corpuscles are fairly abundant, and epithelia from the convoluted and straight collecting tubules of the kidney are seen in moderate numbers. Epithelia from the ureters and the pelves of the kidneys are constant occurrences.

Connective-tissue shreds are usually found, and may contain some granules of hæmoglobin upon them. Mucus in the form of threads or casts may be present, studded with masses of hæmoglobin. In those cases different salts, especially crystals of calcium oxalate and uric-acid crystals, are seen. In cases which have lasted a long time needles and plates of hæmatoidin may be found.

CHYLURIA.

Chyluria is characterized by the milky-white appearance of the urine, similar to milk or to chyle; this appearance it retains on account of the molecular division of the fat which it contains, even if left standing for days. In some cases, though not in all, chylous urine has a pink tinge, due to the red blood-corpuscles frequently present.

Two varieties of the affection are recognized: The first, or tropical form, occurs almost exclusively in hot climates, and is due to an invasion of the blood and urinary tract by a parasite—the *Filaria sanguinis hominis;* the second, or non-tropical form, is not due to a parasite, and is so rare that but little is known about it.

In most cases chylous urine contains coagula, due to a large amount of fibrin which is usually present. These clots form in the bladder, and may be so abundant as to give rise to distressing symptoms when voided.

The features of a chylous urine are illustrated in Fig. 116. The case from which the illustration was drawn was that of a young man, thirty-three years of age, a native of Porto Rico, who had lived in the United States for nine years. Three years before he presented himself for examination he went to his native country for two weeks, and then returned to the United States. Two months after returning he noticed a milky appearance of his urine. The urine cleared up after a short time, and remained clear for more than two years, when it again became milky. The only symptoms he complained of, when he first came under observation, were pain in the back and a slight frontal headache. In appearance the patient was thin and delicate-looking. Upon physical examination nothing could be discovered except a slightly enlarged liver.

Features Found in Urine.—The appearance of the urine was that of milk in which slightly colored, pink coagula were suspended. The clots were numerous and greatly varied in size, the largest being removed from the bottle with difficulty. They had various shapes, some resembling cysts. The specific gravity was 1.015, the reaction slightly acid, and the urine contained one-half of one per cent of albumin.

Under the microscope the clots proved to be masses of fibrin, embedded in which large numbers of red blood-corpuscles were found, and, in a few, also small plates of hæmatoidin. In every field not obscured by the fibrin, red blood-corpuscles were very abundant, lying in groups, as well as singly, partly of a yellowish color, containing hæmoglobin, and partly colorless. Crenated red blood-corpuscles were present in moderate numbers, and many were seen edgewise.

Besides these, minute fat-globules and -granules were extremely numerous, partly in smaller or larger masses, partly lying irregularly throughout the field. Nowhere could larger fat-globules be seen. In some of the drops examined a number of parasites, the embryonal forms of the *Filaria sanguinis*, could easily be discovered; they were of different sizes. In one drop a group of five, embedded in or perhaps surrounded by a mass of fat-globules, was found. One small body, apparently an ovum, was also seen.

The other features were pus-corpuscles and epithelia from the ureters and the middle layers of the bladder. Neither the pus-corpuscles nor the epithelia were found in every drop, it being necessary to examine a number of drops before they were seen. Connective-tissue shreds were present, though not in every drop. No salts whatever could be discovered under the microscope.

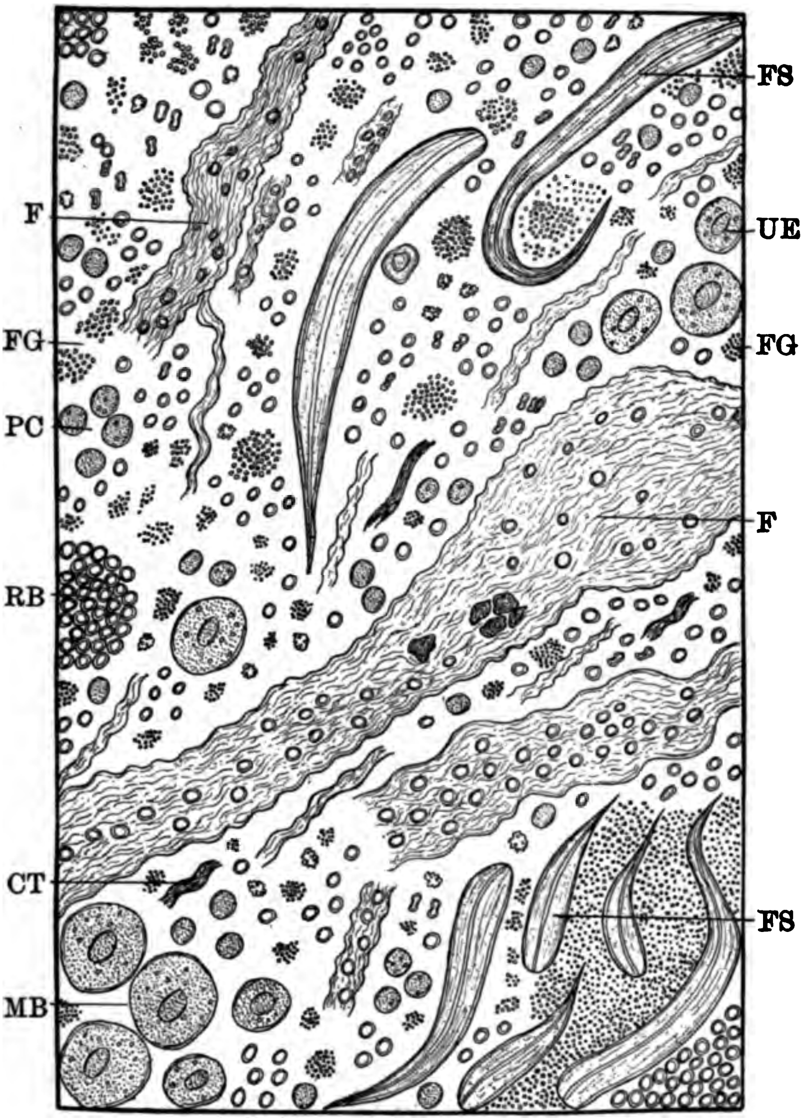

FIG. 116.—CHYLURIA, CATARRHAL CYSTITIS (× 500).

FG, Free fat-globules; *RB*. red blood-corpuscles; *F*, fibrin, with red blood-corpuscles and hæmatoidin crystals; *FS*, Filaria sanguinis; *PC*, pus-corpuscles; *UE*, epithelium from the ureter; *MB*, epithelia from the middle layers of the bladder; *CT*, connective-tissue shred.

III. *MALIGNANT TUMORS OF THE KIDNEY.*

Malignant tumors of the kidney are fortunately rare, but do occur, and both sarcomata and carcinomata are met with. The former may be found at all ages, while the latter, which in the kidneys seem to be of still rarer occurrence than sarcomata, are usually seen in persons more advanced in years. The diagnosis of sarcoma of the kidney can be positively made from the examination of the urine, while that of cancer might perhaps be suspected, but can hardly be made with the same degree of certainty as when it occurs in the bladder.

Clinical Symptoms.—When a malignant tumor has lasted for some time, the clinical features will become pronounced enough to lead one at least to suspect its presence, but in the early stages its symptoms are not well defined; though even at this time characteristic features may be found in the urine. Pain, referred either to the region of the affected kidney or, less clearly defined, radiating to neighboring organs, will usually be the earliest symptom. It is mostly of a severe character, and may be paroxysmally increased.

Very soon a tumor in the region of the kidney can be mapped out, the patient becomes anæmic and cachectic, and gradually loses strength. If not relieved by surgical procedures, the general symptoms become more pronounced, and the disease, as a rule, ends fatally within one or two years, although cases of sarcoma which have lasted four or five years are on record.

Appearance of Urine.—The appearance of urine is not characteristic. Since symptoms of inflammation soon develop, the specific gravity, color, and amount of urine voided will vary with the intensity of the inflammation. Hemorrhages, either constant or recurring at irregular intervals, soon appear, and the urine then has the pronounced reddish or brown color, due to the blood. Albumin is always present in varying amount.

SARCOMA.

Sarcoma of the kidney may be found in children as well as in adults, the youngest case seen by the author and diagnosed from the urine having been in a boy of four years, the oldest in a man of sixty-five years. Although the macroscopical appearance of the urine may vary considerably, the microscopical features are usually characteristic enough to admit of a positive diagnosis. In two cases the examination of the urine gave the first evidence of the disease, the clinical symptoms of the patient not being at first clear; by careful examination of the patient, however, a tumor of the kidney could soon be mapped out, and further developments proved the correctness of the diagnosis.

Features Found in Urine.—That sarcoma of the kidney can be diagnosed from the urine was first shown by Carl Heitzmann, and a number of cases were published by him in the year 1888. Since then other cases have been seen by the author, and autopsies have left no doubt of the correctness of his assertions. In order positively to diagnose sarcoma, we must find large shreds of connective tissue as well as numerous characteristic sarcoma corpuscles in the urine, and therefore an ulceration must have taken place. It is not impossible that these corpuscles may appear in the urine before ulceration has set in, perhaps by emigration; but unless they are very numerous, a positive diagnosis should not be given if large connective-tissue shreds are not found at the same time. It is well known that pus-corpuscles not only vary in size in different individuals, but also to a certain degree in the same individual, and that pus-corpuscles, which are as yet not fully formed and appear as small, compact, or vacuoled bodies, may be found. These should not be mistaken for sarcoma corpuscles.

The features found in a urinary sediment in sarcoma of the kidney are depicted in Fig. 117.

We see extremely large shreds of connective tissue, which in places appear more coarsely granular than usually, and may form regular coils in different portions. Occasionally these shreds will contain a small number of inflammatory corpuscles. Besides the shreds, small, globular, coarsely granular, glistening, even homogeneous corpuscles, in which the nuclei are not seen on account of the coarse granulation, larger than red blood-corpuscles and smaller than pus-corpuscles, are found in large numbers; these are the sarcoma corpuscles. They are not only found singly, scattered throughout the field, but in variously sized, sometimes large groups. These corpuscles are so different in appearance from the larger, in these cases almost invariably pale pus-corpuscles, as to become noticeable at first glance. Being the elements seen in the tumor, they will never appear in any other disease.

Besides these features, we find the evidences of a more or less severe inflammation, either with or without hemorrhage. In the case under consideration, red blood-corpuscles were not numerous, but pus-corpuscles were present in fairly large numbers, many containing fat-globules, showing chronicity. These pus-corpuscles were almost without exception finely granular, and in some one or more nuclei were plainly visible, their appearance being different from the sarcoma corpuscles. Epithelia from the convoluted as well as the straight collecting tubules of the kidney, many containing fat-globules, were present in large num-

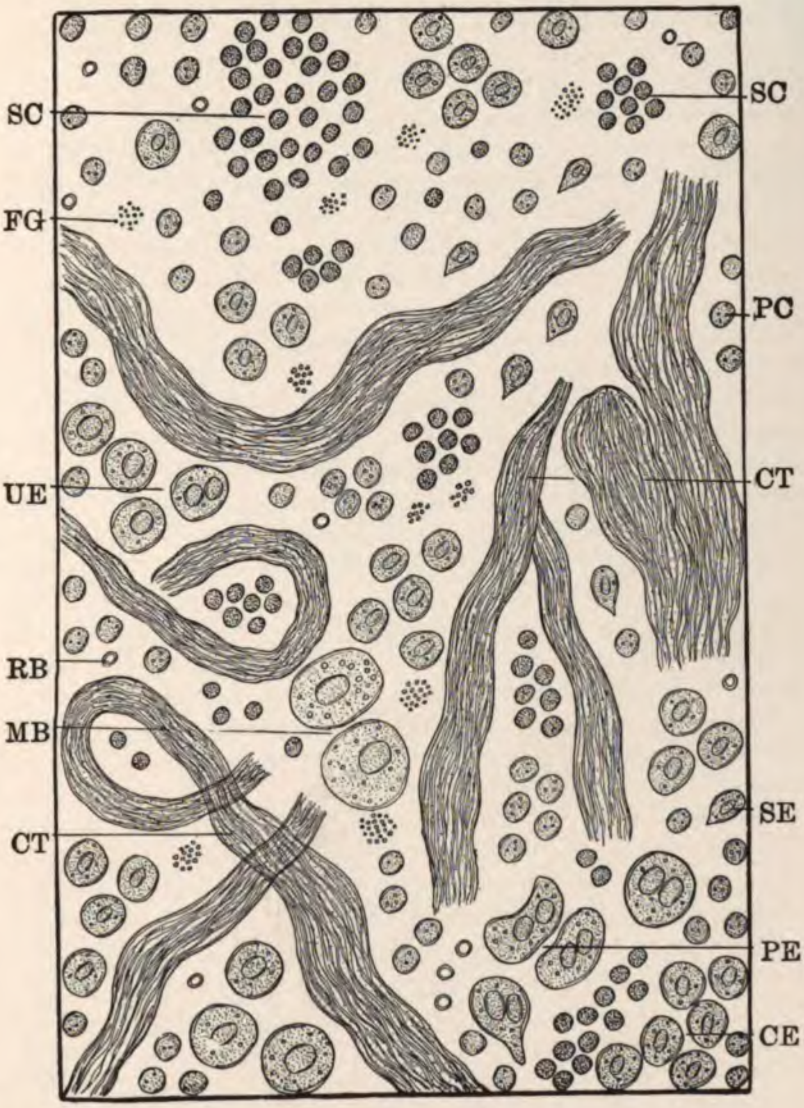

FIG. 117.—SARCOMA OF KIDNEY, CHRONIC PYELITIS AND CATARRHAL CYSTITIS (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles; *SC*, sarcoma corpuscles; *CE*, epithelia from the convoluted tubules of the kidney; *SE*, epithelium from the straight collecting tubules of the kidney; *UE*, epithelia from the ureter; *PE*, epithelia from the pelvis of the kidney; *MB*, epithelia from the middle layers of the bladder; *CT*, connective-tissue shreds; *FG*, free fat-globules.

bers, and groups of free fat-globules were also quite abundant. Epithelia from the pelvis of the kidney could be seen, and in many of them the endogenous new-formations of pus-corpuscles, indicating pressure, were present. Epithelia from the ureter and the middle layers of the bladder completed the features.

Not infrequently a parenchymatous nephritis may be present, and then casts, especially of the granular and fatty variety, will be found.

CANCER.

In cancer of the kidney, a positive diagnosis cannot be made so easily from the simple examination of the urine. When a large number of irregular connective-tissue shreds, containing inflammatory corpuscles, and perhaps also larger, coarsely granular, frequently multinucleated epithelia are found, together with all the evidences of a chronic inflammation, cancer can undoubtedly be suspected, and the clinical symptoms will soon clear up the diagnosis. In rare cases we may find distinct cancer nests, similar to those to be described in cancer of the bladder.

CHAPTER XVII.

DISEASES OF THE BLADDER.

I. *INFLAMMATIONS OF THE BLADDER.*

According to the degrees of intensity, inflammation of the bladder—cystitis—may be divided into catarrhal, suppurative, and ulcerative. The inflammation may be either acute, subacute, or chronic, and may affect either small portions of the mucous membrane of the bladder only, or almost the whole.

The pathological changes in catarrhal inflammation of the bladder are the same as those found in any mucous membrane, and have been described in the previous chapter. In severe inflammations ulcers may be formed, which may become quite extensive, and in rare cases even lead to perforation. Occasionally abscesses will form in the wall of the bladder.

Causes.—The causes of a cystitis, which may be either primary or secondary, are numerous. Primary cystitis may be due either to exposure to cold, to chemical irritation, or to traumata. That a simple exposure to cold may cause a cystitis, often quite severe in character, cannot be denied. Among the chemical irritants different remedial agents, such as turpentine, copaiba, cantharides, and strong mineral acids, may be mentioned. Alcoholic stimulants in large amount may cause mild attacks, as well as certain articles of diet, such as asparagus.

One of the most common causes of cystitis is the passage into the bladder of instruments, such as catheters or sounds, which have not been thoroughly disinfected, so that pyogenic bacteria are introduced in large numbers. Again, traumata of different kinds are often responsible for the development of a cystitis.

Secondary cystitis is at least as frequent as the primary form, and is often due to an extension of the inflammatory process from one or other of the genito-urinary organs. Gonorrhœa is a common cause of cystitis, in the first days of the disease as well as later on. Prostatitis, hypertrophy of the prostate gland, seminal vesiculitis, vaginitis, cervicitis, and parametritis, as well as perimetritis, may all cause it. Again, inflammations of the bladder may be produced by an inflammation of the kidney, pelvis, and ureter, the process gradually extending downward. Indeed, it is rare that a secondary cystitis, though mild in character, does not accompany a nephritis or pyelo-nephritis, even in acute cases. In chronic cases, such an accompanying inflammation is always present.

That other affections of the bladder, such as tumors or calculi in the bladder, will soon cause an inflammation, is evident. In many other diseases, such as the different infectious and contagious diseases, it may occur at any time. Retention of the urine must be looked upon as an important cause.

In most cases, though not necessarily in all, micro-organisms in varying numbers will be present. In the mild acute cases, they may be absent entirely, or be present in small numbers only, while in the more pronounced cases they are always numerous. As a rule, both cocci and bacilli are found, though one or the other may predominate or even exist alone. The varieties of the micro-organisms which may be present in the bladder cannot always be determined, since some of those seen when the urine is examined are undoubtedly of secondary origin. Among the cocci, the different staphylococci—staphylococcus pyogenes aureus, albus, and citreus—as well as the streptococci pyogenes are common. The micrococcus ureæ is often found in large numbers, and a variety of sarcina, called sarcina urinæ, somewhat smaller than the usual form, is not rarely seen. In gonorrhœal cystitis, the gonococcus is present.

Among the bacilli, the bacillus coli communis, the typhoid bacillus, the bacillus ureæ, and the urobacillus liquefaciens septicus, occur. In some cases leptothrix threads are abundant. It has been claimed that the bacillus coli communis is more frequently found in cystitis than any other one bacillus, though the number of bacilli described is quite large.

In the cases of so-called bacteriuria, bacteria of various forms may be present in enormous numbers in the bladder, and their origin cannot always be determined. It is certain that bacteria alone will not cause cystitis, but when an irritation of some kind exists they can set up a severe inflammation. The reaction of the urine does not necessarily need to be alkaline when micro-organisms have developed; but on the contrary, some, as the bacillus coli communis, are frequently found with an acid reaction.

Clinical Symptoms.—The symptoms seen in cystitis vary considerably with the severity and acuteness of the attack. An intense acute inflammation may be ushered in by chills, followed by moderately high fever and all the concomitant symptoms of the same. In milder cases fever will not be present. Frequent micturition invariably exists; this varies considerably with the intensity of the inflammation, and in the severe cases there is a constant desire to urinate, although only a few drops may be voided at a time. More or less intense pain is never absent. The pain may be most pronounced at or just before the beginning of micturition, be somewhat diminished during the flow of urine, and again become more severe at the end of micturition. At other times the flow of urine seems to increase the pain, which is diminished immediately after. A certain amount of pain or discomfort almost invariably exists irrespective of urination, and may radiate to the back, thighs, scrotum, and penis. It may be most severe in the perineum. Pressure upon the bladder, as well as the passage of a catheter or other instrument, always causes more suffering.

In chronic cases which are comparatively mild in character, frequent micturition, sometimes not very pronounced, with a feeling of discomfort, may be the only symptom. When a cystitis has lasted for a long time the coats of the bladder become thickened, sometimes to a great degree. In such cases the bladder is never entirely emptied, and incontinence may exist, so that the urine will dribble away continually.

Appearance of Urine.—The appearance of the urine varies. In the mild cases, when few or no bacteria are present, it may be perfectly transparent; but as soon as bacteria in moderate or large numbers have developed, it is more or less turbid. The specific gravity also differs, being normal in mild cases and increased or diminished in the severer forms. Albumin is never entirely absent in these cases, since it will always be found whenever pus-corpuscles are seen in the urine. In mild cases, however, no more than a trace, sometimes very faint, can be discovered, while in the more intense cases it may exist in large amount. The reaction of the urine may be acid or alkaline. In mild acute cystitis, even when a few bacteria are seen, it may be acid, though, as a rule, only faintly so. In chronic cases, on the other hand, the urine is always more or less alkaline, and the alkalinity may be marked.

CATARRHAL CYSTITIS.

Microscopical Features.—The microscopical features in cystitis differ in the acute and chronic cases, as well as with the intensity of the inflammation, and are always characteristic on account of the presence of bladder epithelia. Pus-corpuscles, epithelia from the bladder, and mucus-threads are never absent, though their amount differs in the different cases.

Acute Catarrhal Cystitis (Fig. 118).—In an acute catarrhal cystitis of moderate severity the reaction of the urine may still be slightly acid, and salts will usually be found under the microscope, though they are not abundant. Those most commonly seen are crystals of calcium oxalate of

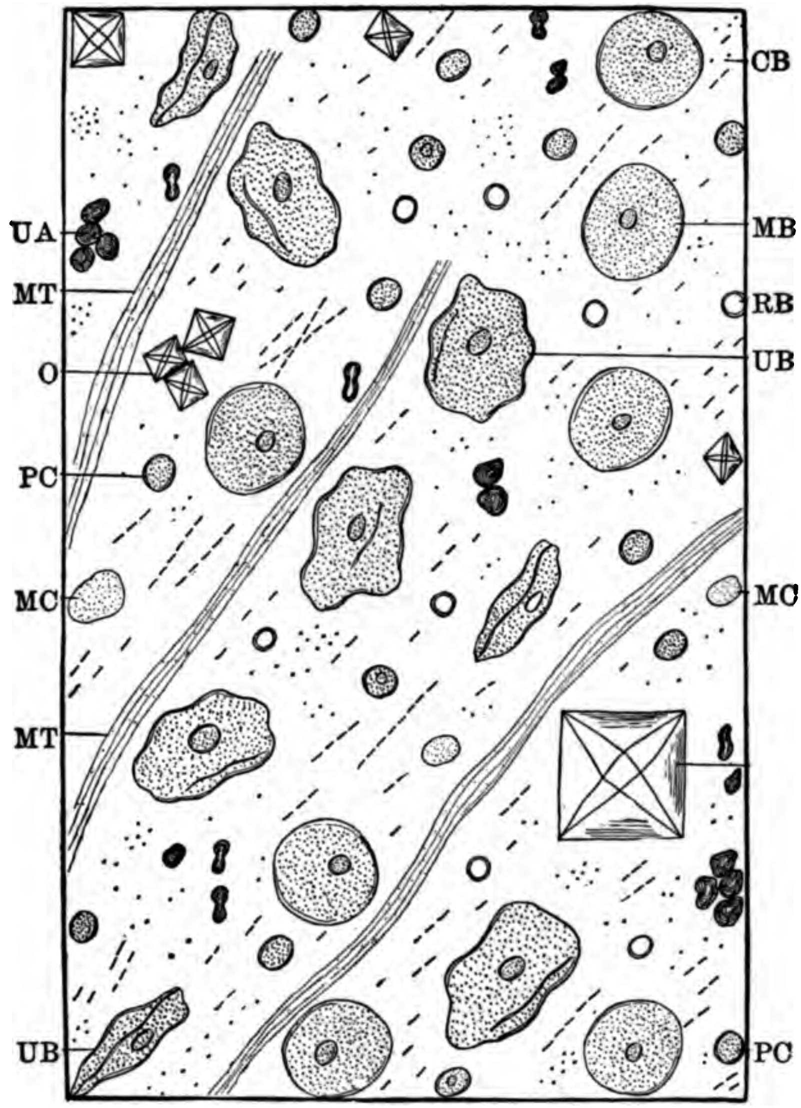

FIG. 118.—ACUTE CATARRHAL CYSTITIS (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles; *O*, calcium oxalate; *UA*, ammonium urate; *UB*, epithelia from the upper layers of the bladder; *MB*, epithelia from the middle layers of the bladder; *MT*, mucus-threads; *MC*, mucus-corpuscles; *CB*, bacilli and cocci.

different sizes, present in almost every field. Even in those cases, however, which still give an acid reaction, globules of ammonium urate; partly the dumb-bell form of ammonium urate *in statu nascenti*, partly small, but fully formed globules, are seen.

Pus-corpuscles are never absent, as without them no diagnosis of inflammation is possible; but their number varies, and the mildest cases show perhaps only two, three, or four in every field. The more intense the inflammation, the more numerous are the pus-corpuscles. Red blood-corpuscles are present in every case of acute cystitis, and also vary in number to a great degree, but, unless hemorrhages have occurred, are never abundant. In hemorrhages, which are rare in these acute cases and are usually found only when the cystitis is due to calculi, tumors, parasites, or a severe trauma, the red blood-corpuscles may be so abundant as to obscure the other features.

The diagnosis of a cystitis depends entirely upon the presence of the characteristic epithelia from the different layers of the bladder. As previously explained, the bladder has stratified epithelium, the different strata of which contain different epithelia. The upper layers are lined with flat, the middle with cuboidal, and the deepest covering, one layer only, with columnar epithelia. The flat epithelia are desquamated in perfect health, though to a small degree only, and when these are present alone in the urine, without any pus-corpuscles or cuboidal epithelia, the diagnosis of cystitis must never be made. As soon as the cuboidal epithelia are found, we can be certain of a pathological process in the bladder; the more pronounced, the more numerous they are.

In an acute catarrhal cystitis the flat epithelia from the upper layers and the cuboidal from the middle layers are always present together, and the more flat epithelia we find in comparison with the cuboidal, the milder the case. In such cases pus-corpuscles are scanty. When the flat and cuboidal epithelia are present in equal numbers, the inflammation is not very severe, but when the cuboidal epithelia are more abundant than the flat, pus-corpuscles will also be more numerous and the inflammation is more intense. We do not expect to find columnar epithelia, unless the inflammatory process has extended to the deepest layer, and has become very pronounced.

The sizes of the different epithelia vary in a small degree only in the different cases, therefore can always be diagnosed. Care must be taken not to mistake folded epithelia from the upper layers for columnar epithelia, which they sometimes resemble; they are, however, somewhat more irregular, always paler, and more finely granular than those from the deepest layer.

Mucus in the form of threads and corpuscles can be found in almost every case, but is more abundant in the severer inflammations. Mucus-threads are pale, and consist of fine, sometimes hardly perceptible fibres. They should never be mistaken for connective-tissue shreds—which we do not expect to find unless the case is intense or hemorrhages occur—since they are pale, finely striated, and the individual fibres usually run quite parallel. When large, mucus-threads may branch off and sometimes fill the greater part of the field. Besides the threads, mucus-corpuscles are also found in varying numbers. Such corpuscles are pale, more or less irregular in outline, finely granular, and do not contain a nucleus. They may have the size of pus-corpuscles, but are often considerably larger. Even in the milder cases of cystitis the so-called cylindroids or mucus-casts—pale, delicate, striated formations—can also be seen.

The only other features which may be found in these cases are bacteria. Their number has little significance as to the severity of the inflammation, since even in severe inflammations they may be scanty, while they may be abundant in a mild case.

Chronic Catarrhal Cystitis (Fig. 119).—In chronic catarrhal cystitis, the reaction of the urine is usually alkaline, and the more chronic the case, the more pronounced is this reaction. The sediment generally contains the different varieties of phosphates, both complete and incomplete triple, as well as star-shaped simple phosphates. Globules of ammonium urate are often quite abundant.

Pus-corpuscles vary in number according to the intensity of the inflammation, and in many small, glistening fat-granules and -globules will be found. Sometimes they contain dark brown granules of pigment. In the more intense cases pus-corpuscles are numerous, and are frequently swollen, hydropic, or disintegrated. In purely chronic cases red blood-corpuscles are scanty or entirely absent. When acute exacerbations or hemorrhages ensue, they become considerably more numerous.

Epithelia are always present in greater or less amount, but their relative numbers are somewhat different from those found in acute cystitis. While in the latter flat epithelia from the upper layers are quite abundant, they are either entirely absent in the chronic cases, or are seen in small numbers only; this is one of the differential points of diagnosis. Epithelia from the upper layers, when present in large numbers, denote either an acute case or an acute exacerbation of a chronic inflammation. Cuboidal epithelia from the middle layers are always found in varying numbers, many containing fat-granules or -globules. Columnar epithelia from the deepest layer are seen in the severer cases only, and then in small numbers. Free fat-globules are always present.

Mucus-threads and -corpuscles are constant features in chronic ca-

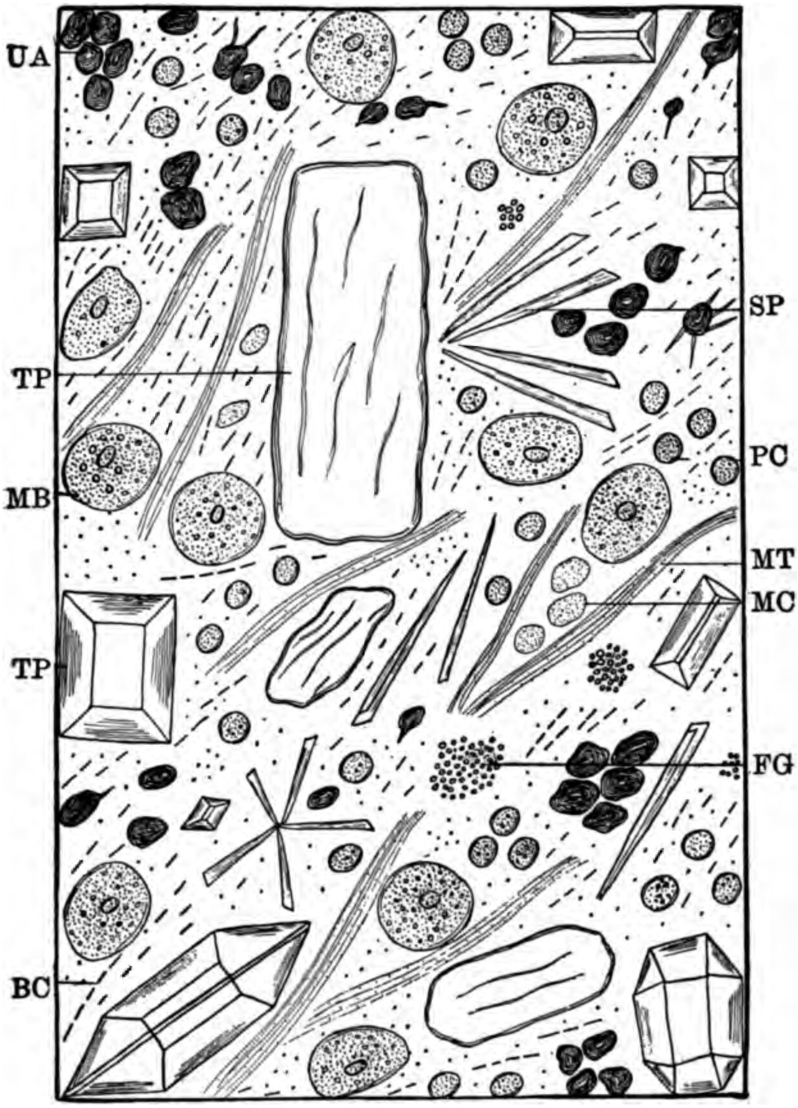

FIG. 119.—CHRONIC CATARRHAL CYSTITIS (× 500).

UA, Ammonium urate; *TP*, triple phosphates; *SP*, simple phosphates; *PC*, pus-corpuscles; *MB*, epithelia from the middle layers of the bladder, containing fat-globules; *MT*, mucus-threads; *MC*, mucus-corpuscles; *BC*, bacilli and cocci; *FG*, free fat-globules.

tarrhal cystitis. In cases having a highly alkaline reaction, the urine is ropy and a jelly-like, viscid mass is present, sometimes so pronounced as to compose the greater part of the sediment. A urine containing such masses always has an ammoniacal odor, and the alkaline salts are extremely numerous. Besides the salts and bacteria, such a jelly-like mass consists of strings of mucus, sometimes filling entire fields of the microscope. In many of these cases neither pus-corpuscles nor epithelia can be recognized to any great degree, having become hydropic, pale, and apparently changed to mucus-corpuscles. The appearance of a urine containing such masses is so characteristic to the naked eye that a diagnosis of chronic cystitis can, in many cases, be made without a microscopical examination. Bacteria are never absent in chronic inflammations, and are usually abundant.

Subacute Catarrhal Cystitis.—The features found in a subacute catarrhal cystitis are a moderate number of red blood-corpuscles, pus-corpuscles, as a rule not abundant, a few epithelia from the upper layers of the bladder, a moderate number from the middle layers, a few fat-globules, and a moderate amount of mucus. The reaction in such cases is usually faintly alkaline.

ULCERATIVE CYSTITIS.

The development of ulcers in the bladder is not rare, and traumata of different kinds are perhaps the most frequent causes. With the presence of calculi and parasites in the bladder, but especially in tuberculosis in any part of the genito-urinary tract, ulcerative cystitis is of common occurrence. In pronounced cases such a urine has an intensely putrescent odor and is very turbid.

Microscopical Features.—**Acute Ulcerative Cystitis** (Fig. 120).—Under the microscope the features of an acute ulcerative cystitis are the following:

The number of pus-corpuscles varies considerably, and they are not necessarily abundant. Red blood-corpuscles are always fairly numerous, and in many cases even hemorrhages exist. Epithelia from the bladder are abundant, and present from all three layers; the columnar epithelia from the deepest layer, usually absent in catarrhal inflammation, are often almost as abundant as those from the middle layers.

Connective-tissue shreds are found in large numbers, some of the shreds being large, while others are only of small size. These shreds are of moderate refraction, and consist of wavy, irregular fibres. The difference between them and mucus-threads, which are also present in varying numbers and are much paler than the former, is plain.

Bacteria are numerous in all these cases, and zoöglœa-masses are invariably found. These masses are often large and numerous, and are never seen to such an extent in simple catarrhal cystitis. Their diagnosis is easy, and when large groups are present around connective-tissue shreds, in fresh urine, the existence of an ulcer is almost certain. The salts vary considerably in amount in acute cases, and at times they are found in small numbers only.

Chronic Ulcerative Cystitis (Fig. 121).—Alkaline salts, especially phosphates, are abundant. Pus-corpuscles are present in moderate number, but red blood-corpuscles are usually scanty. Epithelia from the upper layers of the bladder are either entirely absent or scanty, though transitional epithelia may be found. Cuboidal and columnar epithelia are abundant, the latter being often almost as numerous as the former. Fat-globules and -granules, both in free groups and in the pus-corpuscles and epithelia, are always seen. Connective-tissue shreds are just as abundant as in acute cases, while mucus-threads and -corpuscles are more numerous. Zoöglœa-masses are never absent, and may attain large sizes. Other bacteria are also found in large numbers.

When the diagnosis of a chronic ulcerative cystitis has become clear from the above features, and when, as not infrequently happens, attacks of hemorrhage, even if only mild, occur; when, furthermore, no evidences of calculi or parasites are found, an examination for tubercle bacilli should always be made. In a number of cases, where the clinical symptoms were vague, but an ulcerative cystitis was present, examination for tubercle bacilli revealed the existence of a *tuberculosis* in the urinary tract, and at once cleared up the case.

In one case, which was examined by the author, the ulcerative cystitis was produced by actinomyces. The urine contained a number of small granular masses, apparent to the naked eye, and upon examination these were found to consist of the characteristic club-shaped conglomerations of actinomyces, previously described.

SUPPURATIVE CYSTITIS.

Suppurative cystitis is comparatively rare. The diagnosis can be made if pus-corpuscles are numerous and epithelia from the different layers of the bladder abundant. Connective-tissue shreds are always present and red blood-corpuscles quite numerous. In such cases bacteria will be seen in larger numbers, but the zoöglœa-masses, which are found in every case of ulcerative cystitis, are not present, or, if so, not pronounced. The differential diagnosis between an abscess and an ulcer must, however, be made chiefly from the comparative numbers of pus-corpuscles, which in an abscess are considerably more abundant.

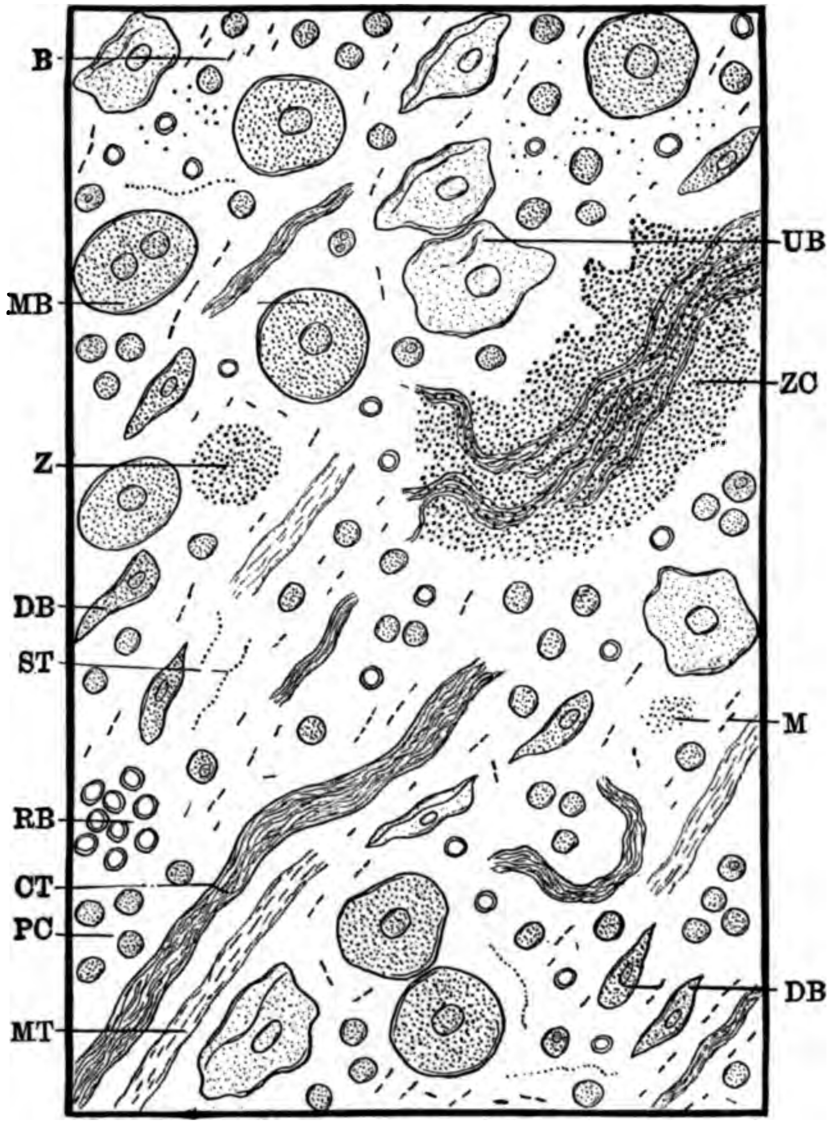

Fig. 120.—Acute Ulcerative Cystitis (× 500).

RB, **Red blood-corpuscles;** ***PC***, **pus-corpuscles;** ***UB***, **epithelia from the upper layers of the bladder;** ***MB***, **epithelia from the middle layers of the bladder;** ***DB***, **epithelia from the deepest layer of the bladder;** ***CT***, **connective-tissue shreds;** ***MT***, **mucus-threads;** ***Z***, **zoöglœa-masses;** ***ZC***, **connective-tissue shreds with zoöglœa-masses;** ***M***, **micrococci;** ***St***, **streptococci;** ***B***, **bacilli.**

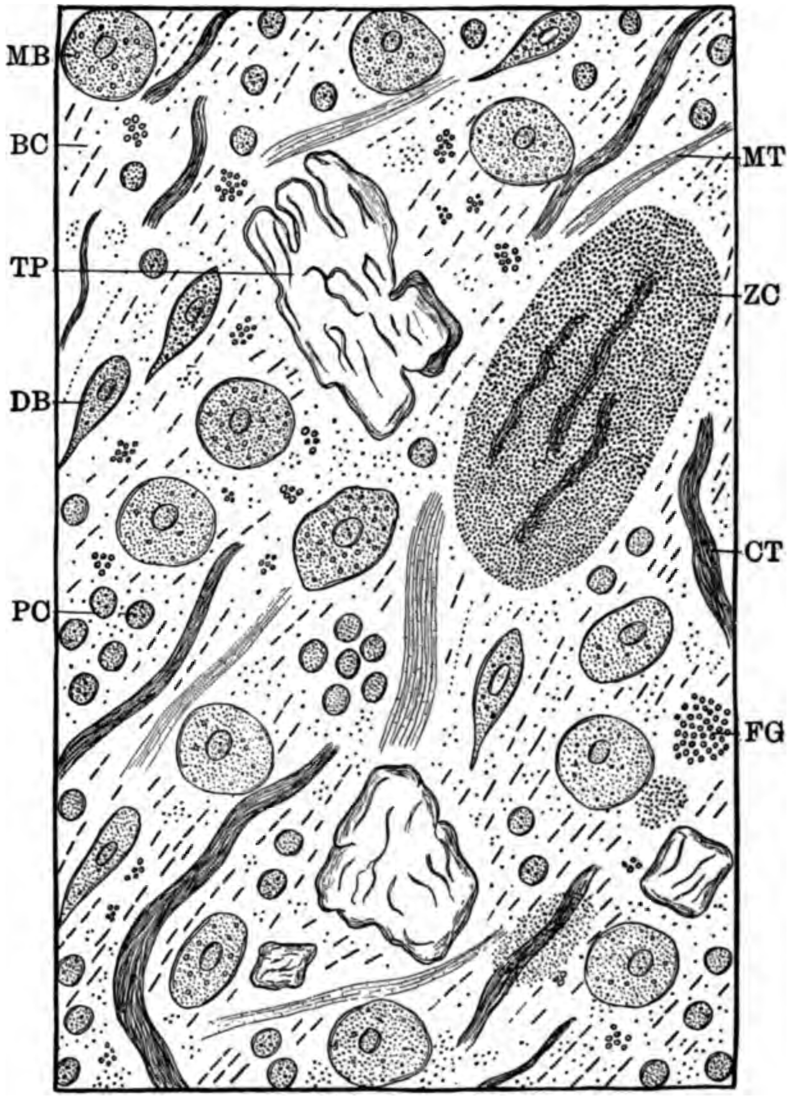

FIG. 121.—CHRONIC ULCERATIVE CYSTITIS (× 500).

PC, Pus-corpuscles, some containing fat-globules; *MB*, epithelia from the middle layers of the bladder, some containing fat-globules; *DB*, epithelia from the deepest layer of the bladder; *TP*, incomplete triple phosphate; *CT*, connective-tissue shreds; *MT*, mucus-thread; *FG*, free fat-globules; *Z*, zoöglœa-mass; *BC*, bacilli and cocci; *ZC*, zoöglœa-masses with connective-tissue shreds.

PERICYSTITIS.

When an inflammation is present around the bladder, instead of in the wall of the bladder proper, and pressure is exerted upon that organ, the epithelia from the middle layers of the bladder may show changes in a pronounced degree, which have been previously alluded to as endogenous new-formations. Such changes will occur when parametritic exudates exist, pressing upon the bladder, when a tumor is present either in the neighborhood of the bladder or in the wall of the bladder, or even simple extravasations of blood in the wall of the bladder may cause them. Pressure of any kind, no matter how slight, if continued for some time, such as pressure of the uterus upon the bladder, or of the prostate gland on account of hypertrophy of that organ, or inflammations of the seminal vesicles, will all produce such changes.

In simple catarrhal cystitis a small number of epithelia from the middle layers may be found, containing a number of nuclei or even newly formed pus-corpuscles. So long as these formations are scanty, they may be produced by the inflammatory process alone—a fact which has been known for many years. As soon, however, as the epithelia become irritated through pressure of some kind, the endogenous new-formation of pus-corpuscles in the desquamated cuboidal or columnar epithelia is very abundant. One epithelium may contain from two to four or even six such pus-corpuscles, or, instead of them, vacuoles may be seen, or pus-corpuscles and vacuoles in varying numbers.

The features found in a case of pericystitis due to a parametritis are shown in Fig. 122. They are the following:

Pus-corpuscles are present in rather large numbers, and red blood-corpuscles are fairly numerous. Cuboidal epithelia from the middle layers of the bladder are abundant, and in almost every one the endogenous new-formation is plainly visible; smaller cuboidal epithelia from the ureters are present in moderate numbers, some of which also contain endogenous new-formations. In a few of the pus-corpuscles and epithelia fat-globules are seen, and small groups of free fat-globules are also found. Mucus-threads are abundant and large, while connective-tissue shreds are scanty and small.

Besides these features, ciliated columnar epithelia from the mucosa of the uterus and larger irregular epithelia from the cervix uteri are seen, as well as those from the upper and middle layers of the vagina, which, with the pus-corpuscles, are sufficient evidences of an endometritis, cervicitis, and vaginitis.

II. *TUMORS OF THE BLADDER.*

Although many different varieties of tumors may occur in the bladder, the most common, and those which can frequently be diagnosed from an examination of the urine, are benign papilloma and malignant sarcoma and cancer. Myoma is a rare tumor in the bladder, but when present can also be diagnosed, if particles of the tumor appear in the urine. As long as no ulceration has taken place, the presence of a tumor of any kind can only be suspected; but as soon as ulceration has set in and particles of the tumor are found in the urinary sediment, the diagnosis becomes positive.

Clinical Symptoms.—In all tumors of the bladder, benign as well as malignant, one of the first, if not the first, and most pronounced symptoms is hæmaturia, mild in character only at the commencement, and occurring at long intervals, but later becoming more pronounced and more frequent. This hæmaturia may take place at any time, and is just as common during rest as when the patient is active. Besides the hæmaturia, pain is present in many cases, but not in all, being more frequent in malignant than in benign tumors, and radiating to the perineum, the thighs, and the scrotum. In benign growths, pain, if present at all, is rarely pronounced. Frequent micturition may exist quite early in the disease, and becomes more pronounced in the later stages.

Malignant tumors sooner or later will cause general symptoms, and, as a rule, end fatally in the course of one or two years, although cases of undoubted sarcomata have been known to last four or five years.

None of the symptoms here given are at all characteristic, and microscopical examination of the urine must be relied upon for a positive diagnosis. Tumors of the bladder may occur at all ages, a case of papilloma having been diagnosed by the author from the urine of a child of one year.

PAPILLOMA.

Microscopical Features.—The microscopical features in a case of papilloma of the bladder are illustrated in Fig. 123.

Since hemorrhage is of such common occurrence in these tumors, red blood-corpuscles are usually present in the urinary sediment in large numbers. These may be irregularly scattered throughout the field, or are found conglomerated in groups, partly yellowish, containing hæmoglobin, but at the time of examination mostly colorless, with the characteristic double contours. In cases of active hemorrhages, hæmatoblasts, having the appearance of red blood-corpuscles, but only half their size,

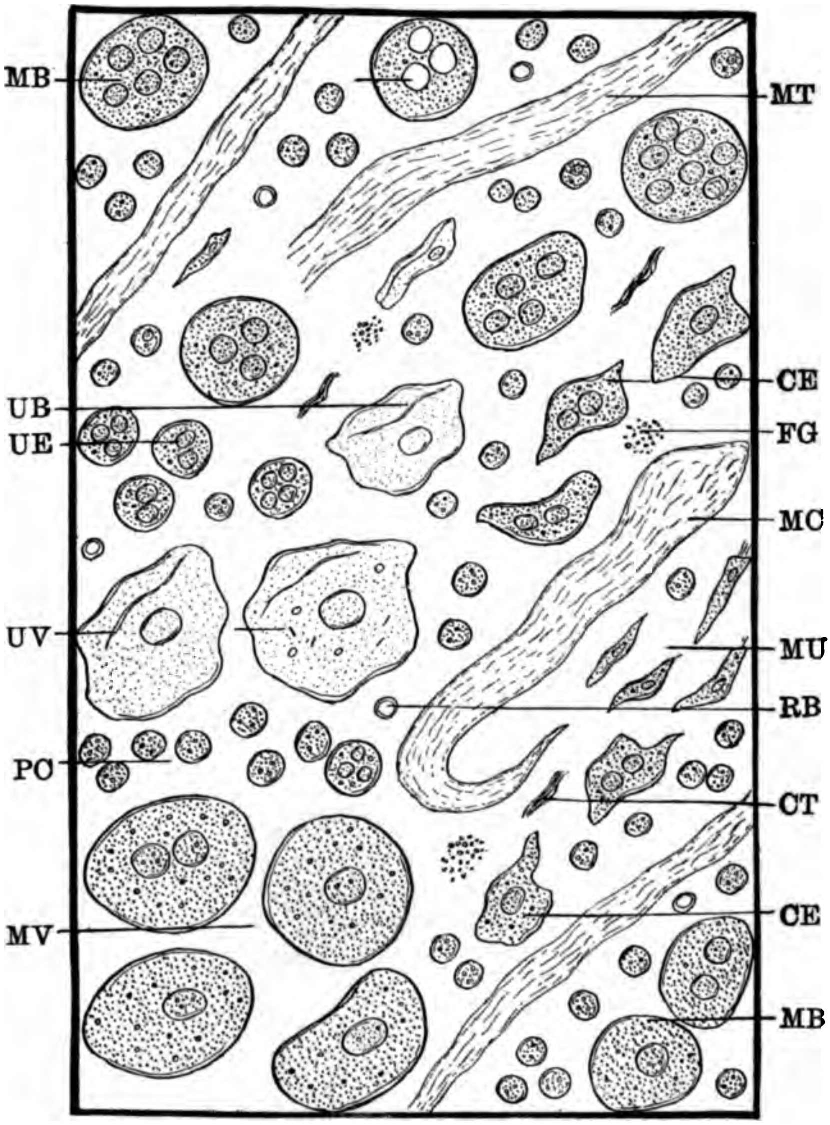

FIG. 122.—PERICYSTITIS, DUE TO PARAMETRITIS (× 500).

RB, Red blood-corpuscle; *PC*, pus-corpuscles; *UB*, epithelium from the upper layers of the bladder; *MB*, epithelia from the middle layers of the bladder, with endogenous new-formations; *UE*, epithelia from the ureter, with endogenous new-formations; *MU*, epithelia from the mucosa uteri; *CE*, epithelia from the cervix uteri; *UV*, epithelia from the upper layers of the vagina; *MV*, epithelia from the middle layers of the vagina; *MT*, mucus-thread; *MC*, mucus-cast; *CT*, connective-tissue shred; *FG*, free fat-globules.

may be abundant. If the latter contain hæmoglobin, so that the double contour is not seen, care must be exercised not to mistake them for fat-globules, or even conidia; they may be found in large groups as well as singly, between the regular-sized blood-corpuscles.

The characteristic features of a papilloma are peculiar connective-tissue shreds, which, as a rule, are abundant. Although variously sized shreds, not differing in any respect from those generally seen in the urine, are present, the larger numbers have an entirely different appearance. They are long, or extremely irregular, frequently branching in different directions, and often assume the shape of coils or knobs. Such shreds are coarsely granular, and not infrequently contain a number of inflammatory corpuscles. Again, they may be found studded with fat-globules of different sizes, some of these being quite large. In rare cases, blood-vessels, either in process of formation or fully formed, some of considerable size, may be contained in them.

The forms in which connective-tissue shreds may be found in the urine when a papilloma exists are sometimes so peculiar that a diagnosis can only be made when smaller and more regular shreds are found. In one case it seemed at first glance as if large parasites of an unknown nature were present, but a more careful examination showed large knobs and coils, in which capillary blood-vessels, filled with blood-corpuscles, were seen coursing in various directions. The individual fibres of such shreds may have entirely disappeared, and the whole shred appears as a mass of coarsely granular protoplasm; these shreds might well be termed protoplasmic outgrowths of connective tissue. The more common varieties of connective-tissue shreds found in papilloma are shown in the illustration.

In all cases of papilloma, epithelia from the different layers of the bladder, more especially the cuboidal and columnar varieties, are quite abundant, and usually are more or less studded with fat-globules, which latter are also seen in small groups. Many of the bladder epithelia contain the endogenous new-formations. Besides these, irregular, coarsely granular epithelia, with endogenous new-formations—the covering epithelia of the papilloma—are also present. These have the size of bladder epithelia, though they are always irregular, and are not characteristic of the papilloma. In none of the cases were the epithelia found adherent to the connective-tissue shreds, and care must be taken not to attempt a diagnosis of a tumor from these epithelia alone.

In every case of papilloma pus-corpuscles are present. They vary in amount with the intensity of the accompanying inflammation, which, though never absent, differs in degree in different cases. As a rule, the pus-corpuscles are present in moderate numbers and are distinct, but sometimes they become massed into pale, irregular degenerated groups, which are not easily diagnosed. In rare cases enormous masses of fibrin are found in the urine—regular fibrinuria. Mucus-threads are always present, though the other features may render them indistinct.

SARCOMA.

As has been described in the previous chapter, a sarcoma can be diagnosed from the urine, when present in any part of the genito-urinary tract. Sarcomata of the bladder, although not common, undoubtedly occur. As in all tumors of the bladder, hemorrhages are frequent in sarcoma, and when the urine is examined during an attack of hemorrhage, the diagnosis becomes more difficult, since no such characteristic connective-tissue shreds as in papilloma are here found.

Microscopical Features.—If blood-corpuscles are present in moderate numbers only at the time of the examination, the other features are distinct enough, and groups of small, glistening, frequently homogeneous, coarsely granular corpuscles, larger than red blood-corpuscles, but smaller than pus-corpuscles, are found in large numbers. These corpuscles, resembling lymph-corpuscles, are the elements characteristic of a small round-celled or lympho-sarcoma. Connective-tissue shreds must, however, always be seen before the diagnosis becomes positive; these shreds may attain large sizes, and frequently contain inflammatory corpuscles. In most cases they do not differ from the shreds commonly found in urine, except by their large size.

The other features seen in a sarcoma of the bladder are the same as those seen in every severe subacute or chronic catarrhal or ulcerative cystitis, epithelia from the deepest layer of the bladder being rarely absent. Many epithelia contain endogenous new-formations, and these are not infrequently seen in the accompanying epithelia from the ureters. Pus-corpuscles and fat-globules in varying numbers, together with mucus-threads, complete the features in these cases.

CARCINOMA.

The varieties of cancer developing in the bladder are principally the villous, the squamous, and the medullary, the first two being more common than the third. Villous or papillary cancer, the so-called cauliflower growth, is probably due in many cases to a secondary malignant change of a previously benign papilloma. This can be proved in those cases in which a tumor, having lasted for years and having always given the characteristics and features of a benign papilloma, becomes changed and assumes the features of malignancy. Such a villous cancer is in reality only

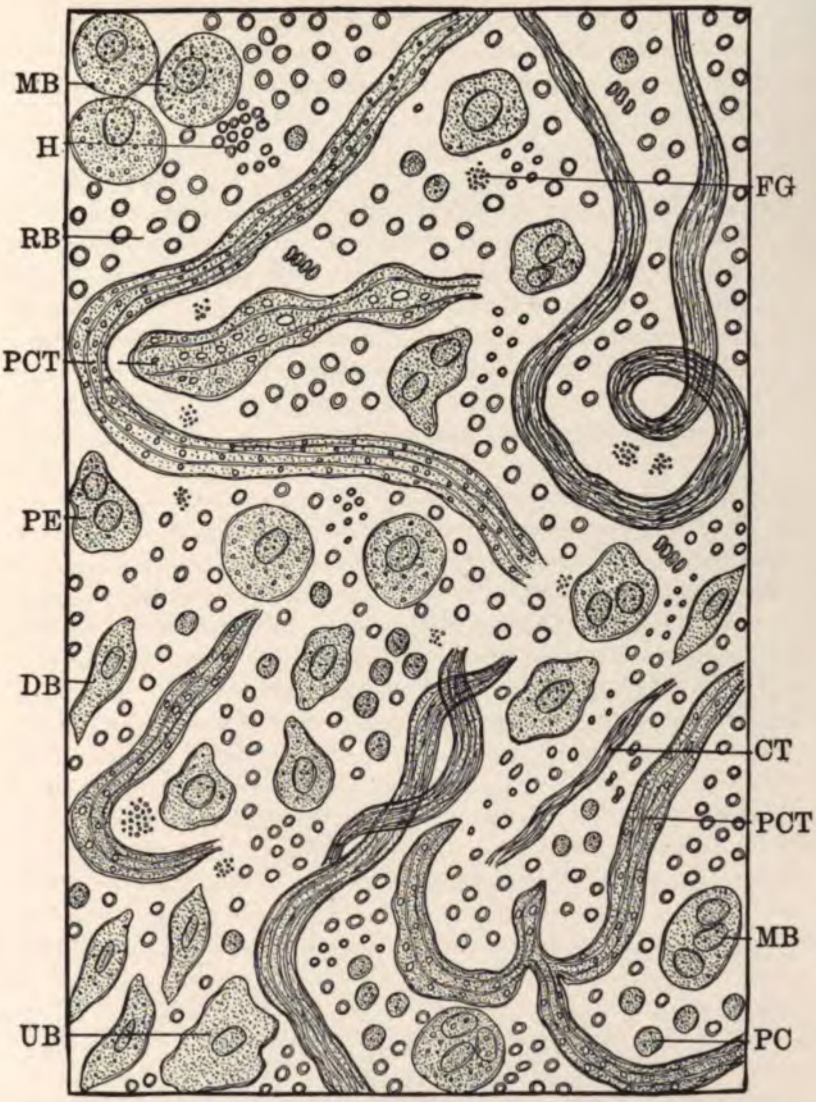

Fig. 123.—Hemorrhage from the Bladder, Due to Papilloma of Bladder (× 500).

RB, Red blood-corpuscles; *H*, hæmatoblasts; *PC*, pus-corpuscles; *MB*, epithelia from the middle layers of the bladder, containing fat-globules; *DB*, epithelia from the deepest layer of the bladder; *PE*, covering epithelia of papilloma; *UB*, epithelium from the upper layers of the bladder; *PCT*, connective-tissue shreds from papilloma; *CT*, connective-tissue shred; *FG*, free fat-globules.

a subvariety of a squamous cancer or epithelioma, but seems to be more frequently seen in the bladder than the regular epithelioma. Medullary cancer, perhaps the most malignant, that is, most rapidly fatal of all cancers, does not often develop in the bladder, and if it does, can hardly be distinguished by an examination of the urine, unless large masses of the tumor are cast off.

Microscopical Features.—The features found in a urinary sediment of a case of villous cancer are depicted in Fig. 124.

At the time this urine was examined, there was no active hemorrhage; therefore red blood-corpuscles were not numerous, though some were present. In different fields variously sized, dark brown or even black blood-clots were seen, composed of masses of disintegrated blood-corpuscles. Hæmatoidin crystals, in the form of small plates and needles, the latter also seen in small conglomerations, were present, though not abundant.

The connective-tissue shreds found in villous cancer may be even larger and more irregular than those seen in papilloma, not infrequently having the appearance of cauliflower-like excrescences, or containing large bulbs or knobs. These shreds are always coarsely granular and filled to a greater or less degree with inflammatory corpuscles, more pronounced than in papilloma. Again, a number of these shreds contain large, irregular cancer epithelia, sometimes even small nests, a feature never found in the connective tissue from a papilloma. Capillary blood-vessels, filled with blood-corpuscles, are sometimes found in these shreds, and may pervade their entire length.

The original fibrous structure of the connective-tissue shreds has become changed, and only scanty fibres are present, the shred frequently appearing as a mass of coarsely granular protoplasm. Connective-tissue masses with a pronounced epithelial covering may perhaps occur in the urine in rare cases, but the detached masses from the tumor are usually changed, being broken down more or less completely, so that an epithelial covering is rarely seen.

Besides the epithelia from the middle and deepest layers of the bladder, containing fat-globules and endogenous new-formations, large numbers of irregular, coarsely granular epithelia, partly single, partly in groups, are present; these also contain fat-globules and endogenous new-formations, and are the cancer epithelia. As long as these epithelia are seen alone, without other evidences of cancer, no diagnosis of a malignant tumor can be made, since they cannot be differentiated from other epithelia, as, for instance, those found in papilloma. In pronounced cases of cancer, however, variously sized epithelial nests may be seen, containing three, four, or more cancer epithelia, and as soon as these are found the diagnosis of a cancer becomes positive, even though the connective-tissue shreds should not be as characteristic as above described. Pus-corpuscles are always present in moderate or large numbers.

Not only can a villous cancer be diagnosed, as just described, but also a regular epithelioma. In such cases the urine may contain epithelial masses showing a pronounced concentric arrangement, and even different degenerations of the epithelia, especially cornification, producing shining, irregular masses—the so-called cancer pearls—may be present. All the other features remain the same.

The positive diagnosis of medullary cancer from the examination of urine is difficult, though the presence of a cancer of some kind can, as a rule, be made from features similar to those described.

When a tumor in the bladder has existed for some time, secondary inflammations of the ureter, the pelves of the kidneys, and the kidneys frequently develop sooner or later, and may become pronounced. In the kidney both interstitial or catarrhal and parenchymatous or croupous inflammation may appear. The urine then shows all the features of such an inflammation, in addition to those of the tumor. In the case of a child one year of age, in which a papilloma of the bladder existed, all the features of a subacute croupous nephritis were also found, and the case proved fatal in a short time.

III. *PARASITES IN THE BLADDER.*

That a large number of micro-organisms of different kinds may not infrequently be found in the bladder, has already been mentioned. Symptoms of a more or less pronounced cystitis will sooner or later appear in almost all those cases.

Animal parasites are also occasionally found in the bladder, among these being *echinococci*, *actinomyces*, *distoma hæmatobium*, and *filaria sanguinis*, as well as *ascaris lumbricoides*, *strongylus gigas*, and *oxyuris vermicularis*. The diagnosis of these parasites is possible only when either their ova or the parasites themselves can be discovered in the urine. Many of these will invade the bladder only secondarily, being present in other organs, as the kidney or pelvis, or find their way into the bladder through the urethra.

In every case of this kind, either hemorrhage or inflammations of varying degrees of intensity will sooner or later develop, with all the characteristic features in the urine. Ulcers are often due to such parasites, as, for instance, in the case of actinomycosis of the bladder previously mentioned.

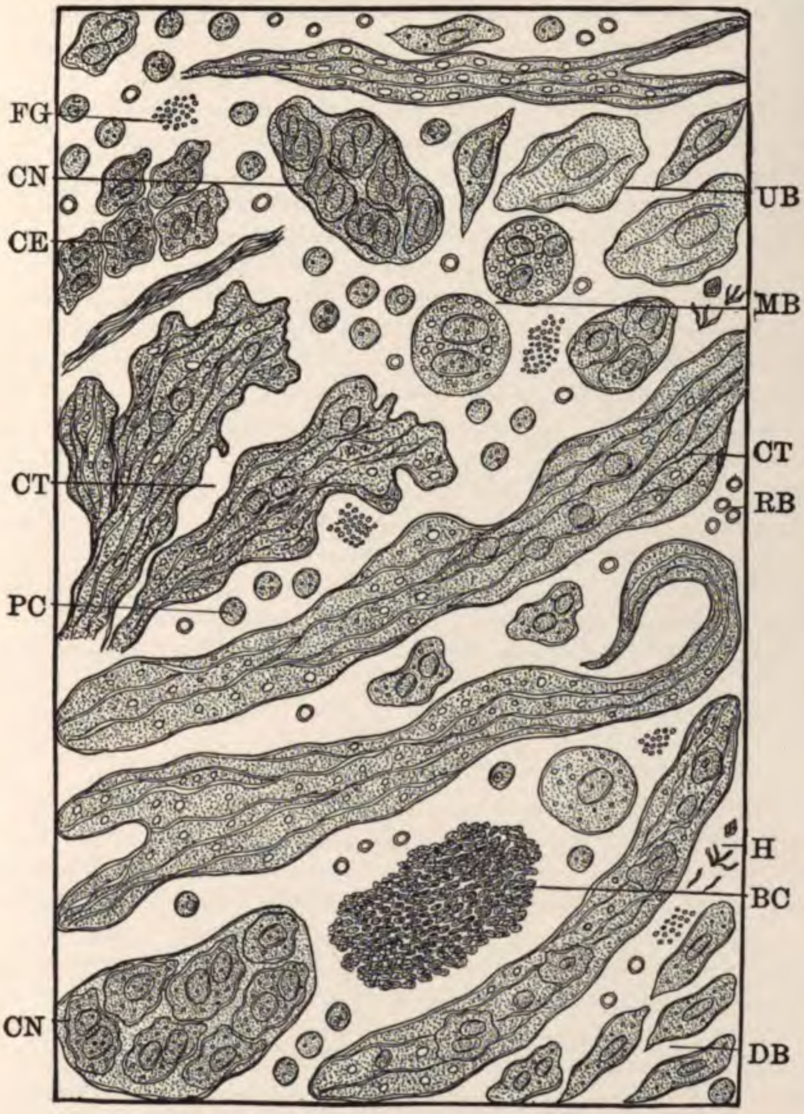

FIG. 124.—VILLOUS CANCER OF THE BLADDER (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles; *UB*, epithelia from the upper layers of the bladder; *MB*, epithelia from the middle layers of the bladder, containing fat-globules and endogenous new-formations; *DB*, epithelia from the deepest layer of the bladder; *CE*, cancer epithelia; *CN*, cancer nests; *CT*, connective-tissue shreds; *H*, hæmatoidin crystals; *BC*, blood-clot; *FG*, free fat-globules.

CHAPTER XVIII.

DISEASES OF THE SEXUAL ORGANS.

DIAGNOSIS of diseases of the sexual organs by microscopical examination of the urine must of necessity be limited; it is not of so great practical importance as in diseases of the urinary organs, since the clinical symptoms are in many cases sufficiently clear. There are, however, cases where the examination of the urine will either corroborate a suspected diagnosis or may even lead to the clearing up of the case when the clinical symptoms are not plain. This will naturally be of more common occurrence in diseases of the male than of the female tract, in which latter, examination of the patient is, as a rule, sufficient for the diagnosis.

In the male, inflammations of the urethra, the prostate gland, and the seminal vesicles can be diagnosed from urine examination, while in the female those of the vagina are easily diagnosed, and sometimes also those of the cervix of the uterus and the uterine mucosa.

URETHRITIS

Acute Urethritis.—The clinical symptoms of an acute urethritis, whether gonorrhœal or non-gonorrhœal, are so evident that an examination of the urine is never required to clear up the case. When the urine is examined for other purposes at the time such a urethritis is present, large numbers of urethral epithelia are always found. In the first days of a urethritis the irregular, flat epithelia from the upper layers are more abundant, but soon the cuboidal and columnar epithelia are seen. Pus-corpuscles are present to a varying degree in every case.

Chronic Urethritis.—The symptoms of a chronic urethritis, especially when of a mild character, may be so slight that an examination of the urine will help to clear up the diagnosis.

In many or these cases conglomerations of mucus with pus-corpuscles and epithelia—the so-called gleet-threads—are found, even though they are scanty. Under the microscope these threads (Fig. 57) consist of a varying amount of mucus, both fibres and corpuscles, from the mucous glands of the urethra; pus-corpuscles, which are abundant in the more pronounced, but may be quite scanty in the mild cases, and urethral epithelia, which also vary in number. Besides these features, epithelia from the prostate gland are almost invariably present, and are usually more numerous than the urethral, which latter may at times not be found at all. The larger numbers of pus-corpuscles and epithelia are seen studded with small fat-globules, and these may also be seen upon and between the mucus-threads. If gleet-threads are not present, irregular urethral epithelia in small numbers, with pus-corpusles, mucus-strings, and prostatic epithelia, are seen in many cases of chronic urethritis.

When an ulceration or stricture exists in the urethra, the urine, as a rule, shows some features. In an ulceration, red blood-corpuscles in at least moderate numbers, pus-corpuscles, bacteria—especially the zoöglœa-masses—urethral epithelia, mostly the cuboidal and columnar varieties together, and connective-tissue shreds are never absent. As the prostate gland almost invariably becomes involved in these cases, prostatic epithelia are also present.

In stricture of a mild character, small connective-tissue shreds, with a few epithelia from the urethra and prostate gland, and a few pus-corpuscles, are not infrequently seen, although there may be no features whatever in the urine of such cases. The urethral epithelia may have two or even more nuclei.

PROSTATITIS.

The diagnosis of a prostatitis from the urine is undoubtedly of greater importance than that of a urethritis, since, especially in the mild chronic cases, the clinical symptoms may not be sufficiently pronounced.

Causes.—The causes of a prostatitis are numerous, though probably the most frequent cause of an acute inflammation is an acute urethritis. The passage of unclean instruments, such as sounds or catheters, injections of chemical agents, or any irritant or injury of whatever kind, such as may be due to horseback or bicycle riding, may cause a prostatitis, as well as simple exposure to cold and wet. In the course of febrile diseases it also develops occasionally.

Chronic prostatitis may be produced by stricture of the urethra, masturbation, excesses in venery, hemorrhoids, constipation, or by inflammations of the neighboring organs.

Clinical Symptoms.—An acute prostatitis, if severe, may be ushered in by chills and fever, followed by discomfort or pain in the perineal region and frequent micturition. The pain is usually increased upon motion, and the perineum is found to be sensitive upon pressure.

In chronic prostatitis the symptoms may be slight, the principal one perhaps being the occasional discharge of a small amount of a clear, viscid fluid, constituting the so-called prostatorrhœa; this flow is usually increased upon defecation. Besides this, slight discomfort and tenderness in the perineum, frequent micturition, and slight pain at the end of urination may be present. Enlargement of the gland may cause more or less retention of urine.

Features Found in Urine.—The appearance of the urine varies considerably with the intensity of the inflammation, and is not characteristic. In acute cases slight or more pronounced hemorrhages may take place, and cause the urine to assume a darker color; when considerable pus is present it will be more or less turbid, and also contain a varying amount of albumin. In mild chronic cases the urine may be perfectly clear.

When such a urine is examined for albumin, it must not be forgotten that whenever pus-corpuscles and red blood-corpuscles are present albumin will always be found, its amount depending upon the amount of pus and blood, so that in cases of abscesses or hemorrhages the urine may contain considerable albumin, and faint traces are rarely absent when there is any inflammation of the prostate gland. It is evident, therefore, how important a microscopical examination of the urine becomes in all these cases, since such an examination alone will determine whether the kidneys are inflamed, and this be the source of albumin, or whether the albumin is due simply to the prostatitis.

Acute Prostatitis.—In an acute prostatitis of moderate severity, the features found in the urinary sediment are red blood-corpuscles in varying numbers, pus-corpuscles, mucus, and epithelia from the prostate gland. Red blood-corpuscles are never absent in an acute inflammation, and are numerous when hemorrhages occur, as is sometimes the case. Pus-corpuscles vary in number according to the degree of intensity of the inflammation. Mucus, in the form of threads and corpuscles, is always increased, and may be present in large amount.

The characteristic features of a prostatitis are the epithelia. The prostate gland is, as a rule, lined by simple cuboidal epithelium, though occasionally a pseudo-stratified epithelium, partly cuboidal and partly columnar, is seen; while the ducts of the gland are lined by columnar epithelia. The cuboidal epithelia are about twice the diameter of the pus-corpuscles, and are larger than those from the convoluted tubules of the kidney. They have the same size as the cuboidal epithelia from the ureters, and when they are present alone, without the columnar epithelia from the ducts, the comparative number of these, with those of the kidney and pelvis of the kidney, must be taken into consideration. An inflammation of the ureters is almost invariably secondary to a nephritis or pyelitis, and when the epithelia from the kidney or pelvis, or both, are seen, together with a small number of those twice the size of the pus-corpuscles, they are always ureteral. The absence of symptoms of a pyelo-nephritis, but the presence of a varying number of cuboidal epithelia double the size of pus-corpuscles, would show that they are from the prostate gland. Since a prostatitis, especially when it has lasted for some time, may cause a secondary inflammation of the bladder, the ureters, pelvis of the kidney, and kidney, epithelia from all these organs may be present, and here not only the comparative number, but also the clinical symptoms of the case, will have to be taken into consideration to determine the positive source of the epithelia.

On the other hand, in an inflammation of the prostate gland the columnar epithelia from the ducts of the gland are almost invariably present with the cuboidal epithelia in moderate or even large numbers, while the columnar epithelia from the ureters are rarely seen, and then in small numbers only. The columnar epithelia from the pelvis of the kidney, although they vary in size to a certain degree, are always somewhat larger than those from the ducts of the prostate gland and more irregular, so they cannot be mistaken for the latter.

A prostatitis is in most cases associated with inflammation either of the urethra or of the bladder (especially the neck), or both, and the epithelia from these organs will then be associated with those from the prostate gland. Severe cases, as already mentioned, are ascending in character, producing a pyelitis and finally a nephritis, with all the accompanying features of the same.

Acute suppurative prostatitis, or abscess of the prostate gland, is of common occurrence, and its features are illustrated in Fig. 125.

We see here red blood-corpuscles in moderate numbers, and pus-corpuscles in extremely large amount, which not infrequently fill up entire fields of the microscope. Cuboidal epithelia from the prostate gland, as well as columnar epithelia from the ducts, are always present in these cases, and are not infrequently found in groups. Connective-tissue shreds are seen in varying numbers, and unless they are found the diagnosis of an abscess must never be made, even if pus-corpuscles and epithelia are numerous. The latter is the chief point of distinction between a severe, but non-suppurative, prostatitis and an acute abscess. Mucus-threads may be found in large numbers.

When a suppurative prostatitis is the result of a urethritis, which is frequently the case, the irregular epithelia from the urethra will be found accompanying the features just described, and, as a rule, epithelia from the upper and middle layers of the bladder are also present, showing a cystitis. In both the urethral epithelia and the bladder epithelia an endogenous new-formation of pus-corpuscles may be seen.

Chronic Prostatitis.—Chronic prostatitis will give characteristic features under the microscope (Fig. 126).

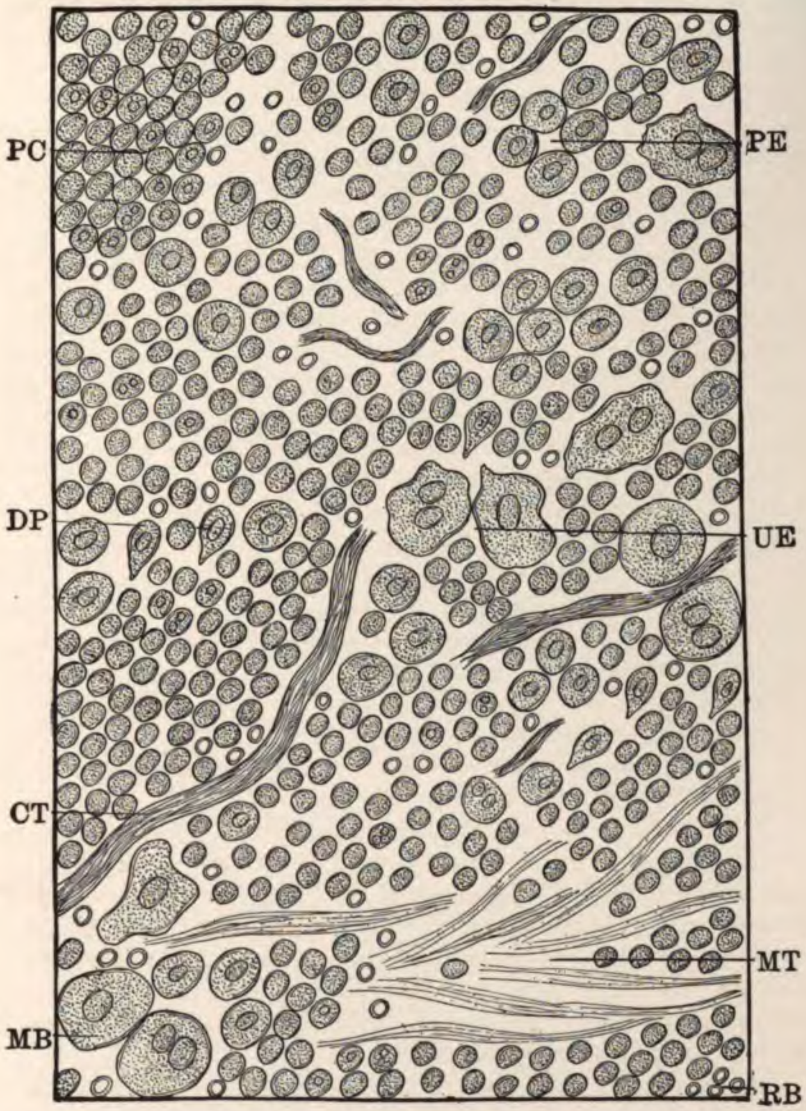

FIG. 125.—ACUTE ABSCESS OF THE PROSTATE GLAND (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles; *PE*, epithelia from the prostate gland; *DP*, epithelia from the ducts of the prostate gland; *UE*, epithelia from the urethra; *CT*, connective-tissue shreds; *MT*, mucus-threads; *MB*, epithelia from the middle layers of the bladder.

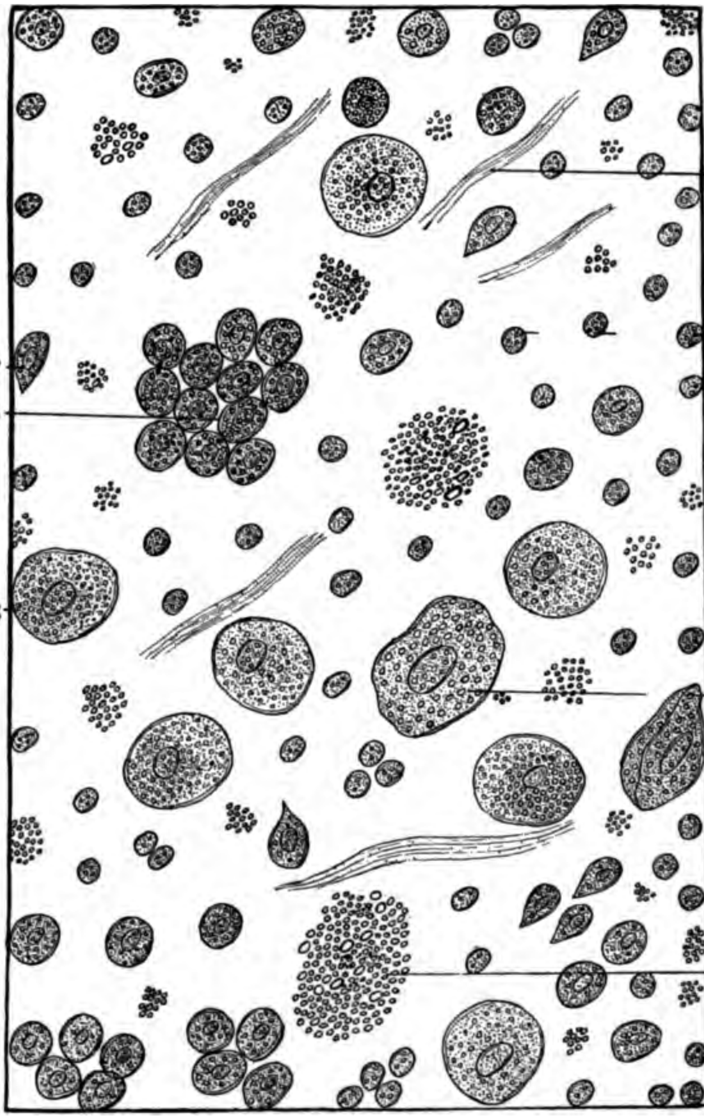

Fig. 126.—Chronic Prostatitis (× 500.)

PC, Pus-corpuscles containing fat-globules; *PE*, epithelia from the prostate gland, containing fat-globules; *DP*, epithelia from the ducts of the prostate gland, containing fat-globules; *MB*, epithelia from the middle layers of the bladder; *NB*, epithelia from the neck of the bladder; *MT*, mucus-threads; *FG*, free fat-globules.

Red blood-corpuscles are here either entirely absent or scanty, and pus-corpuscles are present in moderate numbers only. Cuboidal as well as columnar epithelia from the prostate gland and its ducts are quite abundant, the former being often found in groups of four, five, or more. Both the pus-corpuscles and the epithelia are studded with glistening fat-globules and -granules, which latter also lie free. In the case from which the illustration was drawn, this fatty change was extremely pronounced—more so than is usually the case. Every epithelium and almost every pus-corpuscle were filled with these globules, giving the whole corpuscle a glistening appearance. The free groups of fat-globules were numerous and large, the individual globules in many groups being of considerable size. Mucus-threads were seen in moderate numbers, but connective-tissue shreds were absent.

In this case no urethral epithelia were seen, but the accompanying cystitis was pronounced, so that the epithelia from the bladder were quite abundant. Not only the regular cuboidal epithelia from the middle layers of the bladder, studded with fat-globules, were present, but also larger epithelia from the neck of the bladder. Mention should here be made of the fact that the epithelia from the neck of the bladder are usually larger than those found in the other portions of the bladder, and may even attain the size of vaginal epithelia. These large epithelia are, however, never numerous, are seen only with the other features, and are not studded with bacteria, as is almost invariably the case in the epithelia from the upper layers of the vagina.

Hypertrophy of the prostate gland may give characteristic features in the urine, even before the clinical symptoms are sufficiently pronounced to lead to a suspicion of the affection (Fig. 127). In all these cases the features of a chronic prostatitis are found, usually with a small or moderate number of pus-corpuscles only, but with small connective-tissue shreds, which in many cases are scanty. If the latter are seen with all the evidences of a chronic prostatitis, especially when the age of the patient is above forty or forty-five years, the diagnosis of hypertrophy can be made. When the hypertrophy becomes more pronounced, endogenous new-formations will be seen in the larger numbers of epithelia from the middle layers of the bladder, as well as in those from the urethra and even in a number from the prostate gland and ducts. In these cases prostatic concretions, previously described, are not rarely found.

Tuberculosis.—Tuberculosis of the prostate gland is probably never present alone without an involvement of the neighboring organs, and is a comparatively rare affection. It will always give the symptoms of a prostatitis or an abscess of the prostate gland with a varying number of pus-corpuscles, and not infrequently even connective-tissue shreds. When it is suspected, repeated examinations for tubercle bacilli must be made.

Tumors.—Tumors of the prostate gland are not of rare occurrence, and both sarcoma and cancer are met with, and can be diagnosed from the urine. In sarcoma, the characteristic small, glistening bodies previously described, with large connective-tissue shreds, and the evidences of a chronic prostatitis are seen; while in cancer the connective-tissue shreds and epithelia, described in cancer of the bladder, may be found in the urine. The clinical symptoms must of necessity help the microscopical examination in many of these cases. In some cases neither sarcoma corpuscles nor cancer epithelia can be found, but all the evidences of a pronounced hypertrophy of the prostate are seen in urine, together with large connective-tissue shreds, which of themselves are sufficient cause of suspicion of the presence of a tumor.

SPERMATORRHŒA.

Spermatorrhœa, which in young men is by no means rare, and consists in an occasional involuntary flow of semen, especially at the end of defecation, or even upon urination, cannot infrequently be diagnosed from the urine.

When a urine is to be examined to prove the presence of a spermatorrhœa, it is best to take either the first urine voided in the morning or the last quantity voided during defecation. In such a urine the elements of the sperma, with spermatozoa in large numbers, will be found. In almost all these cases a prostatitis of varying degrees of intensity will exist and give the features under the microscope.

Whenever a prostatitis is found in young men in whom no other cause can be discovered, a suspicion of spermatorrhœa must arise, even when no spermatozoa are seen in the urine first examined. Repeated examinations will invariably show these, and render the diagnosis positive. The clinical symptoms of a chronic prostatitis—that is, an occasional discharge of a clear, viscid fluid, especially in younger men—may not infrequently lead to the mistaken diagnosis of spermatorrhœa, which disease must never be diagnosed without the evidence of a discharge of sperma.

Besides the prostatic epithelia, those from the seminal vesicles and ejaculatory ducts may also be seen in the urine. Mucus is always present in these cases in large amount, and mucus-casts or cylindroids may be abundant. Care must be taken not to mistake these for true hyaline casts from the uriniferous tubules of the kidney, which they sometimes resemble to a marked degree; sharp focusing will always bring out the pale fibres of mucus, thus proving that they are not hyaline casts.

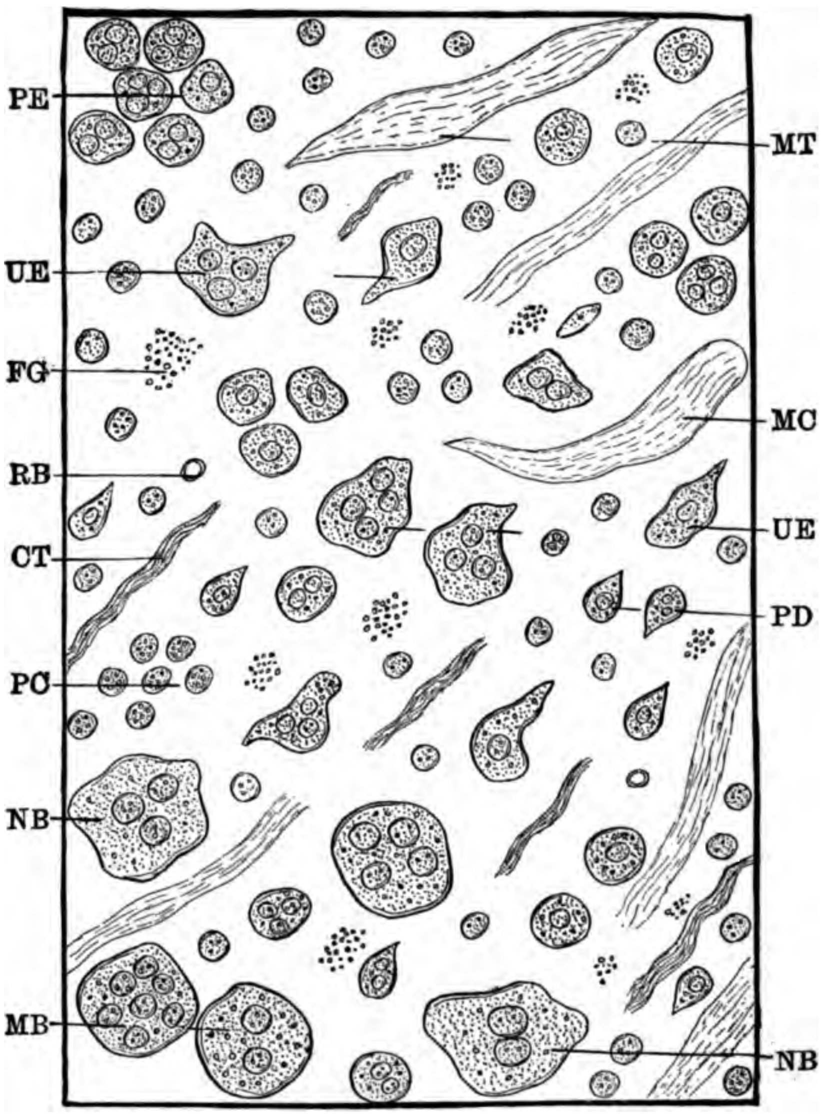

Fig. 127.—Chronic Prostatitis, with Hypertrophy of the Prostate Gland (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles containing fat-globules; *PE*, epithelia from the prostate gland, some with endogenous new-formations; *PD*, epithelia from the ducts of the prostate gland; *UE*, epithelia from the urethra with endogenous new-formations and fat-globules; *MB*, epithelia from the middle layers of the bladder with endogenous new-formations; *NB*, epithelia from the neck of the bladder; *CT*, connective-tissue shreds; *MT*, mucus-threads; *MC*, mucus-cast; *FG*, free fat-globules.

SEMINAL VESICULITIS.

Seminal vesiculitis, or spermatocystitis, has received considerable attention of late years by many authors, who all agree that the affection is of much more common occurrence than has been supposed. Although frequently of gonorrhœal origin, this is not the exclusive cause of the disease, and Fuller claims that in about one-third of the cases it is tubercular in character. It may also be catarrhal in origin, though most authors believe that the non-gonorrhœal cases are rare.

Clinical Symptoms.—The symptoms of a spermatocystitis are not always well pronounced, and, therefore, may escape detection for years. Disturbances of the sexual functions are most constant, though they vary in different cases. In many there is a marked increase of sexual desire, but no relief is afforded by the coitus. This is, however, not present in every case, and in some there is a diminution or even absence of the desire. Pain may be present in the perineum and upon urination, and there may even be tenesmus. In many cases an intermittent or even constant discharge from the urethra, which is sometimes quite profuse, is present, and some patients will complain of bloody emissions.

It will be seen that neither one of these symptoms is at all characteristic, and rectal examination must be resorted to. This is sometimes successful, but in many cases is not; when the seminal vesicles can be reached, they will be found distended and tender to the touch. A positive diagnosis can be reached only by a microscopical examination, and the seminal fluid will, in all these cases, contain pus-corpuscles, and usually, especially in acute cases, red blood-corpuscles.

Features Found in Urine.—The microscopical examination of the urine will often clear up the case. When the early morning urine, especially the part first voided, or the last urine passed at defecation, is examined, spermatozoa are often found. The features seen in the first morning urine in a case of chronic seminal vesiculitis are illustrated in Fig. 128.

Spermatozoa are here found in large numbers. Some of them have the normal appearance, but others appear changed. The change takes place in the head of the spermatozoön, which becomes larger, round, and granular, and finally may resemble a pus-corpuscle, so that we seem to see pus-corpuscles with tails in such a urine. This change is characteristic of the disease, and is frequently seen, though not always in a pronounced degree. The originally oval head first becomes rounded and then somewhat enlarged and granular. In milder cases no further enlargement takes place, while in the more intense cases a number assume the size of pus-corpuscles, being either coarsely or finely granular. Such a diagnosis of changed spermatozoa should be made only when they are distinct and unbroken, their heads and tails being intact. Broken and distorted heads of spermatozoa, also seen in chronic seminal vesiculitis, are useless for a diagnosis, since they may become broken in urine under normal conditions.

Besides the spermatozoa, pus-corpuscles are always found in such a urine, and may be either scanty or numerous, according to the degree of inflammation. Since suppuration not infrequently occurs in the seminal vesicle, pus-corpuscles may be very numerous. Red blood-corpuscles are almost always present, though their number also varies considerably, being abundant in the more pronounced and scanty in the milder or the chronic cases.

Epithelia from the seminal vesicles and ejaculatory ducts can always be found. The former are small, irregular, non-ciliated; the latter are originally columnar ciliated epithelia, in some of which the cilia will be seen, while in others they are broken off. When they are broken, delicate parallel rods in the interior of the epithelia, near their basal surfaces, may indicate that the epithelia were originally ciliated.

In all cases examined, epithelia from the prostate gland were present, showing that the prostate gland was also inflamed. The numbers of prostatic epithelia will, however, vary considerably, though they are usually fairly abundant, both the cuboidal and columnar epithelia being seen. In the more chronic cases fat-globules are found, both in the epithelia and lying free. Mucus is always greatly increased in these cases, and cylindroids or mucus-casts may be numerous; the mucus-threads sometimes assume large sizes. When suppuration exists, connective-tissue shreds are always present. Epithelia from the urethra and the bladder may accompany the other features.

Hemorrhage from the Seminal Vesicles.—Hemorrhages from the seminal vesicles are not rare, and may be due to traumatism of any kind, as well as to tuberculosis and gonorrhœa. Such a hemorrhage may be primarily caused by excesses in venery, as in the case depicted in Fig. 129, in which it immediately followed excessive sexual indulgence in a previously strong, healthy man, continued for some time, and was followed by an inflammation of the vesicles and prostate gland.

When this urine was examined under the microscope, all the evidences of an active hemorrhage were present: red blood-corpuscles, partly crenated and partly lying edgewise, being abundant, and small hæmatoblasts also being found in moderate numbers; besides these, strings of fibrin were seen in different fields. Small, irregular, columnar epithelia from the seminal vesicles, some of which contained pigment granules, were present in small to moderate numbers, and a few longer, slender,

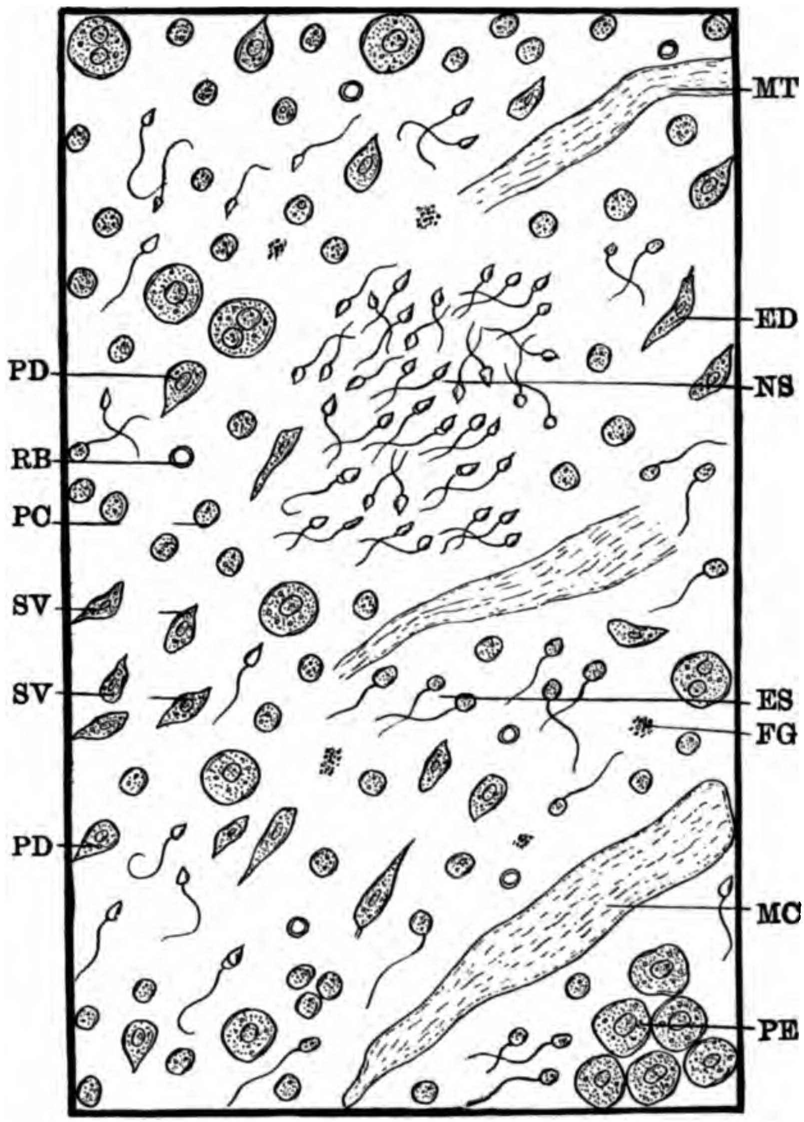

FIG. 128.—CHRONIC SPERMATOCYSTITIS, OR SEMINAL VESICULITIS (× 500).

RB, Red blood-corpuscle; *PC*, pus-corpuscles; *NS*, normal spermatozoa; *ES*, spermatozoa with enlarged and granular heads; *SV*, epithelia from the seminal vesicles; *ED*, epithelium from the ejaculatory ducts; *PE*, epithelia from the prostate gland; *PD*, epithelia from the ducts of the prostate gland; *MT*, mucus-thread; *MC*, mucus-cast; *FG*, free fat-globules.

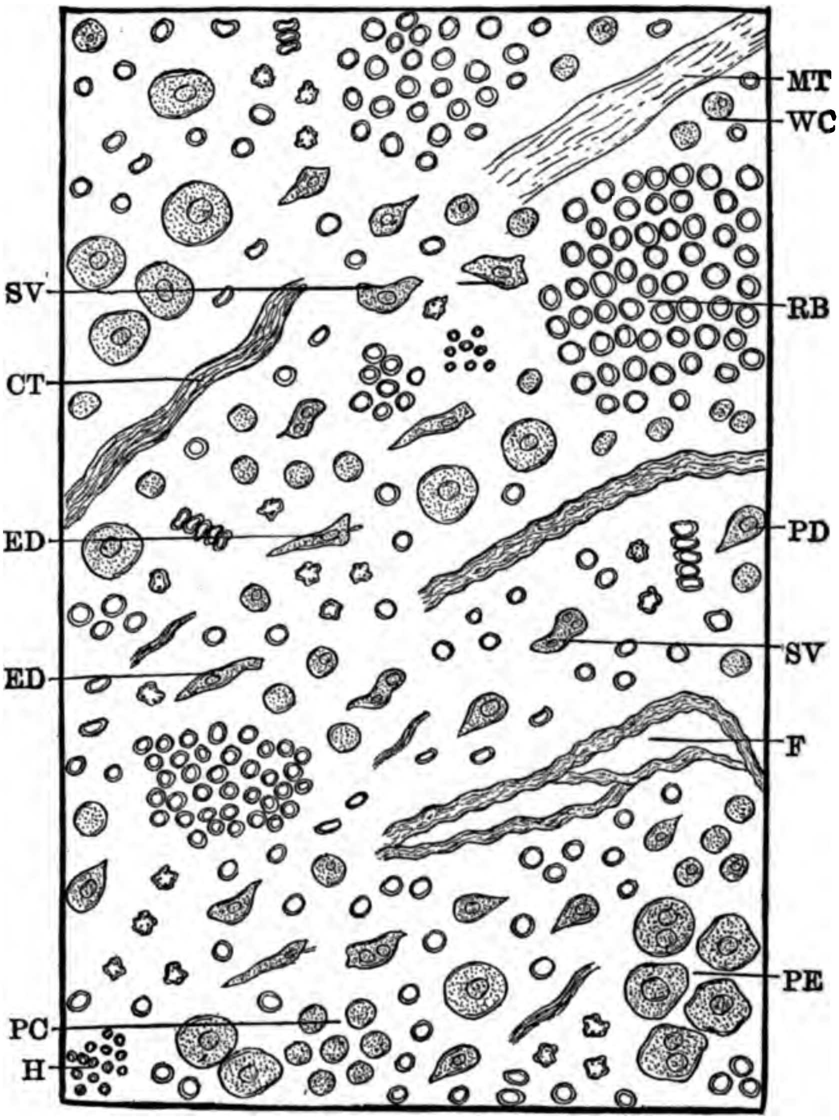

Fig. 129.—Hemorrhage from Seminal Vesicles, with Acute Prostatitis (× 500).

RB, Red blood-corpuscles; *H*, Hæmatoblasts; *WC*, white blood-corpuscles; *PC*, pus-corpuscles; *SV*, epithelia from the seminal vesicles; *ED*, epithelia from the ejaculatory ducts; *PE*, epithelia from the prostate gland; *PD*, epithelium from the ducts of the prostate gland; *F*, strings of fibrin; *CT*, connective-tissue shred; *MT*, mucus-thread.

partly ciliated epithelia from the ejaculatory ducts were also found. Besides these features, the specimen contained pus-corpuscles, connective-tissue shreds, mucus-threads, and cuboidal and columnar epithelia from the prostate gland and its ducts, showing a prostatitis.

In an active hemorrhage of this kind, white blood-corpuscles or leucocytes are invariably present. These cannot be differentiated from pus-corpuscles, and, as long as they are seen in small numbers only, the presence of the latter must not be diagnosed. As soon as these corpuscles are found in moderate numbers, some are undoubtedly pus-corpuscles, and the existence of an inflammation besides the hemorrhage then becomes plain.

VAGINITIS.

Inflammations of the vagina, especially mild chronic cases, are of common occurrence and have little significance, the only symptom being a slight discharge; few women who have borne children are entirely free from this affection. The severer cases may be due to many causes, such as exposure to cold, gonorrhœal infection, or injuries of any kind, or may be secondary to an inflammation of the uterus.

Features Found in Urine.—It is rare that in the urine of a female vaginal epithelia are not found in greater or less amount. Epithelia from the upper layers are shed in a small amount in perfect health, and have no significance; such epithelia may be seen even in small children. So long as the flat epithelia from the upper layers are present alone in small numbers, without cuboidal epithelia from the middle layers and without pus-corpuscles, the diagnosis of a vaginitis cannot be made. As soon, however, as large cuboidal epithelia are also present, a pathological process of some kind exists in the vagina.

Catarrhal Vaginitis.—The common forms of vaginitis seen in the urine are the mild chronic cases, and the features found are shown in Fig. 130.

Pus-corpuscles are always present, but usually in small numbers only. Epithelia from the upper and middle layers of the vagina are quite numerous. These epithelia are considerably larger than those from the bladder, the upper layers being flat, the middle cuboidal. Epithelia from the upper layers are frequently studded with bacilli and cocci, and often contain variously sized extraneous fat-globules. They may be found in groups, which may fill the greater part of the field. Cuboidal epithelia from the middle layers, which in urine usually appear round or oval, though they vary in size sometimes to a great degree, are always larger than those from the bladder, and may also be found in groups. Columnar epithelia from the deepest layer are not seen in these milder cases, but only in severe inflammations or ulcerations.

Besides these epithelia, small cuboidal epithelia, twice the size of pus-corpuscles and exactly similar to those from the prostate gland in the male, are usually present; these are the epithelia from the Bartholinian gland and denote a slight Bartholinitis.

Pus-corpuscles, as well as the different epithelia, contain small fat-globules in varying numbers in all chronic cases. Free fat-globules may also be seen. In most, if not in all cases of vaginitis, micro-organisms, both cocci and bacilli, are found, and are, as a rule, quite abundant. Their presence has no significance, as it is well known that micro-organisms always exist in the vagina, the more pronounced if an inflammation has developed. The characteristics here described are usually seen in urines examined for other reasons and containing other features.

In acute vaginitis red blood-corpuscles as well as pus-corpuscles will be abundant, and vaginal epithelia from the different layers quite numerous. In simple catarrhal vaginitis the flat and cuboidal epithelia are usually present alone, while in vaginitis due to gonorrhœa, and especially in ulcerative vaginitis, columnar epithelia from the deepest layer are also found, and connective-tissue shreds are present in varying amount.

Ulcerative Vaginitis.—The features of ulcerative vaginitis, as seen in urine, are shown in Fig. 131. Flat epithelia from the upper layers, cuboidal epithelia from the middle layers, and columnar epithelia from the deepest layer of the vagina are here seen in moderate numbers, while pus-corpuscles and red blood-corpuscles are fairly numerous. Connective-tissue shreds of varying sizes are present, and some of these are surrounded by micro-organisms in the form of zoöglœa-masses. Mucus-strings and cylindroids, the latter at times difficult of differentiation from hyaline casts, are also seen, while different micro-organisms, both micrococci and bacilli, are scattered throughout the specimen. Epithelia from the Bartholinian gland may be quite abundant.

Besides catarrhal and ulcerative vaginitis, *traumatic vaginitis* due to masturbation may be diagnosed from urine. Here pus-corpuscles are present in small numbers only, and red blood-corpuscles are not numerous; but epithelia from all the layers of the vagina are abundant, the cuboidal from the middle layers and the columnar from the deepest layer being well marked. Epithelia from the Bartholinian gland are also seen in moderate numbers. Epidermal scales, showing corrugated edges, studded with fat-globules and dirt particles, and faintly granular, if at all, are seen in every field. These are derived from the clitoris and nymphæ. Connective-tissue shreds are also seen, though they are not numerous. Micro-organisms and a few fat-globules complete the features.

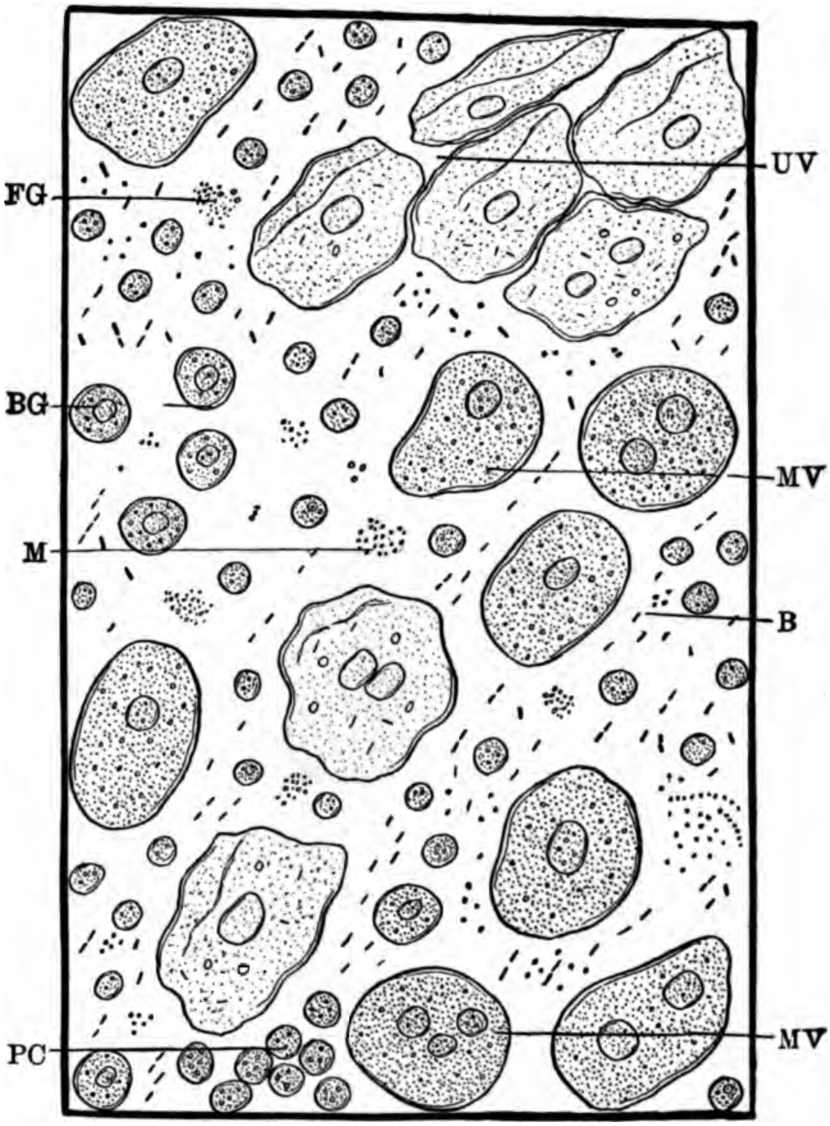

FIG. 130.—CHRONIC CATARRHAL VAGINITIS (× 500).

PC, Pus-corpuscles containing fat-globules; *UV*, epithelia from the upper layers of the vagina; *MV*, epithelia from the middle layers of the vagina, containing fat-globules; *BG*, epithelia from the Bartholinian gland; *FG*, free fat-globules; *B*, bacilli; *M*, micrococci.

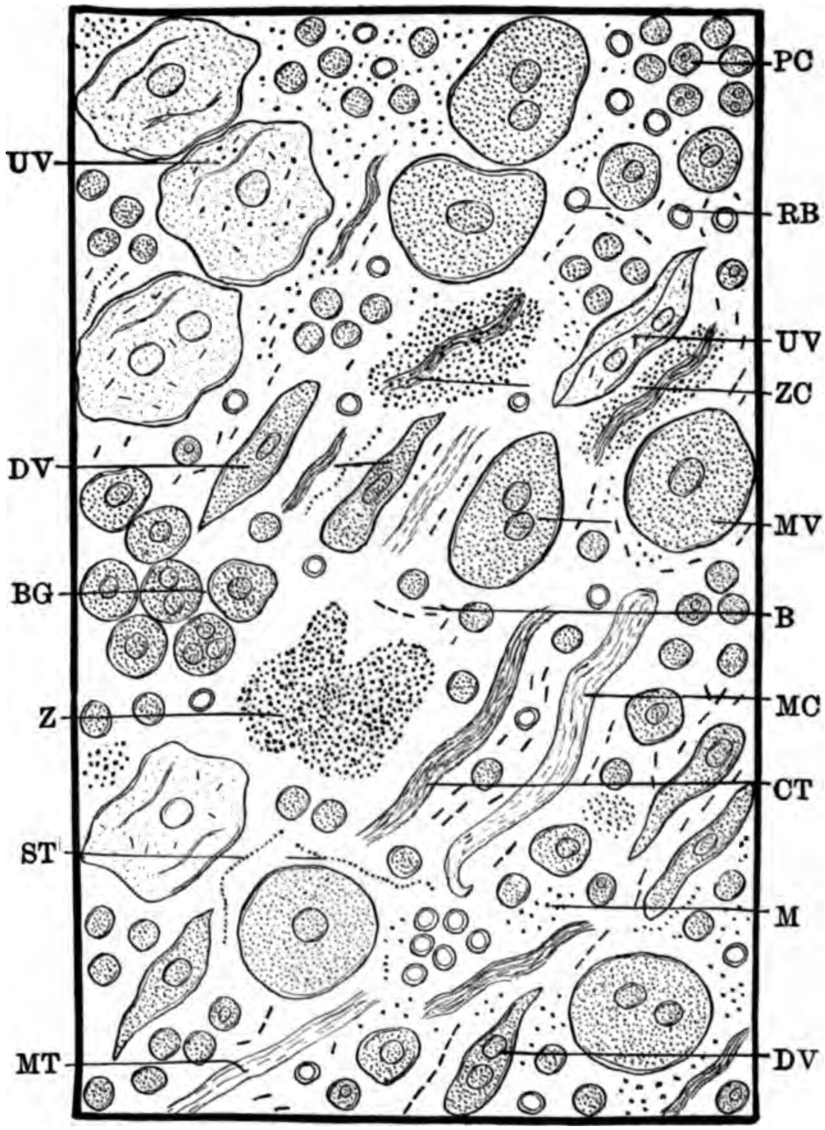

FIG. 131.—ULCERATIVE VAGINITIS (× 500).

RB, Red blood-corpuscles; *PC*, pus-corpuscles; *UV*, epithelia from the upper layers of the vagina; *MV*, epithelia from the middle layers of the vagina; *DV*, epithelia from the deepest layer of the vagina; *BG*, epithelia from the Bartholinian gland; *CT*, connective-tissue shred; *ZC*, zoöglœa-masses surrounding connective-tissue shreds; *MT*, mucus-thread; *MC*, mucus-cast; *Z*, zoöglœa-mass; *M*, scattered micrococci; *St*, Streptococci pyogenes; *B*, bacilli.

Whenever epithelia from the deepest layer and connective-tissue shreds are present, we have all the evidences of a destructive process. Continuous irritation or injury to the parts by masturbation is sufficient to produce these features in small numbers. If an ulcer exists, the pus-corpuscles and epithelia are more numerous; and if traumatism results in hemorrhage, red blood-corpuscles are more abundant. The features here described may be found accidentally when a urine is examined for other pathological conditions, and when seen in that of young girls should always lead to a suspicion of masturbation. The cause of a nervous irritability or neurasthenia is thus not rarely cleared up.

CERVICITIS AND ENDOMETRITIS.

Cervicitis and endometritis may also be diagnosed from the urine, when the different epithelia from the cervix and mucosa of the uterus are present. Epithelia from the cervix uteri are quite large and irregular, while those from the mucosa uteri are columnar ciliated. Both are shown in Fig. 122. The other features of such an inflammation are similar to those seen in any inflammation. In ulcerations or injuries shreds of connective tissue are found. In endometritis we occasionally see pus-corpuscles with cilia from the mucosa uteri, together with the ciliated epithelia.

Tumors from the uterus can be diagnosed from examination of the urine in rare cases only, when a small particle of the tumor is cast off and found in the urine. The features of the tumor are similar to those previously described, and the character of the epithelia will determine the seat of the tumor.

CHAPTER XIX.

DETERMINATION OF THE FUNCTIONAL EFFICIENCY OF THE KIDNEYS.

By

WALTER T. DANNREUTHER, M.D., F.A.C.S.

ASSISTANT PROFESSOR OF GYNECOLOGY, NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL.

WITH a view of determining the functional efficiency of one or both kidneys, and often of estimating the functional capabilities of the patient as well, various methods have been described, which at times may be valuable as aids to the chemical and microscopical examination of the urine. Many of these renal function tests have proved extremely useful to the clinician, and although their scientific exactness is open to question, extensive experience has demonstrated that quite definite conclusions may be drawn from their proper interpretation. A knowledge of the excretory function of the kidneys, as well as the stability of renal sufficiency, is frequently of importance, not only for the diagnosis, but also for the prognosis, and these tests aid materially in obtaining such information. It is imprudent to rely exclusively upon the results of one or more function tests, since they constitute but part of the evidence. Other clinical data, such as the history, physical findings, urine and cystoscopic examinations, and radiography, with its various attributes, must be corroborative and confirmative. A discrepancy in the results of two or more function tests in the same case may be explained by the fact that different areas of the kidneys may be concerned in each instance. One must also bear in mind that lost or deranged function may be either temporary or permanent, and the reading at any one time may not represent the kidney's actual functional ability. Nevertheless, the behavior of the function test is always strongly suggestive.

Renal function tests are serviceable to the medical practitioner by furnishing him a better conception of his patient's general metabolic activities, especially elimination by the kidneys. They likewise indicate the progress as well as the extent of involvement or destruction of kidney tissue in nephritis, cardio-vascular diseases, and other disease processes. To the surgeon they are invaluable, because he may determine thereby with certainty the presence of a healthy kidney on the opposite side before nephrectomy. They also help in the diagnosis of such surgical conditions as urogenital tuberculosis, ureteral stricture, calculus, pyonephrosis, hydronephrosis, etc. There is no other diagnostic procedure which demonstrates a compensatory hyperactivity to the same degree of accuracy. In the so-called "medical nephritis" the excretory inefficiency of the kidneys is generally produced by actual disease of some of their histologic structures, or circulatory alterations, while in "surgical lesions" the impairment of function is usually an end-result of the vicious circle of obstructed drainage, urinary stasis, back-pressure, infection and epithelial disintegration.

As has been shown in the preceding chapters, one of the best methods of determining the integrity of the kidneys themselves is by careful chemical and microscopical examination of the urine. But the collection of separate urines from each kidney entails the use of a catheterizing cystoscope or one of the segregators, and as these instruments are not always available, such examinations are sometimes impossible. When practicable, the specimens should be collected simultaneously and for the same period of time and then carefully examined, and in many cases the condition of each kidney can thus be ascertained. Not only will the character of the pathological process become plain, but also the extent of the lesion, as well as the constitution of the patient at the time of the examination, thus showing whether or not his organism will be able to withstand proposed surgical procedures.

Of the special methods which are used for the determination of renal function, the phenolsulphonephthalein, indigo-carmine, and phloridzin are the most popular and have proven of greatest value. The selected agent is administered to the patient by syringe injection. The material is absorbed, carried by the circulation to the kidneys, and by them filtered from the blood and excreted. The time required before excretion begins, and the quantity eliminated within a given time, vary in direct proportion to the renal activity. That is to say, the more efficient the renal excretory power, the more rapid and more pronounced will be the excretion. Conversely, the more impairment of renal function, the greater the delay of the onset of elimination, and the more will the quantity excreted be reduced. The correlation of urinary obstruction and renal function in conditions such as advanced prostatic hypertrophy must always be taken into account, since large amounts of residual urine may influence all function tests. Under these circumstances the true functional sufficiency of the kidneys cannot be ascertained until a few days after the relief of the urinary obstruction.

The numerous potential sources of error in interpreting the results of renal function tests have undoubtedly been responsible for much of the disfavor with which they have been regarded in the past. The most prolific of these is easily avoided. The intravenous administration is a matter of paramount importance and cannot be too strongly urged, as the agents are thus introduced directly into the economy. Their elimination is consequently rapid and the deductions therefrom are fairly exact. The absorption after subcutaneous or intramuscular injections depends upon capillary proximity to the site of injection, local circulatory activity, the thickness of the walls of the blood-vessels, blood density and osmosis, all of which vary materially in different individuals. This lack of uniformity of absorption in patients adds an element of error easily obviated by intravenous injection, which reduces to the infinitesimal those sources of error that abound after subcutaneous or intramuscular injection. By intravenous injection the dosage is accurate, the selected agent enters the circulation unchanged, and its advent into the renal tissue is prompt and certain, none of which advantages can be claimed for the other methods. Subcutaneous and intramuscular injections of some of the anilin dyes are particularly painful, and this unpleasant feature is also avoided by the intravenous route. In fact, the intravenous administration offers so many advantages over the other methods, and the observations become so much more reliable in consequence, that it should be the only one employed under ordinary circumstances. No untoward results have been noted in an experience of several hundred injections, and the technic is simple. The sole prerequisites for absolute safety are the use of distilled water only in the preparation of the solutions, and perfect sterility.

Cryoscopy of the urine and the methylene-blue test are almost obsolete in this country, and some of the others which have been advocated at various times have not found much favor.

Estimation of the twenty-four hour urea output is often of great importance, but the nitrogenous content of the urine depends upon so many qualifying factors other than the process of elimination that these must always be taken into consideration when viewing such figures as an index of renal function. The significance of the twenty-four hour urea output is greatly augmented by a determination of the non-protein nitrogen, urea nitrogen, creatinin, and uric acid in the blood, and when the urine urea is below the minimum normal of 20 gm. (300 grains), this should always be done as a complementary examination. To elucidate this, a concrete example may be cited. Assuming the twenty-four hour urea to be 17 gm., if the nitrogenous elements of the blood are normal in quantity (non-protein nitrogen, 25 to 30 mg.; urea nitrogen, 12 to 15 mg.; creatinin, 1 to 2 mg.; and uric acid, 2 to 3 mg., in each 100 c.c. of blood), the decrease is probably due to restricted ingestion of proteins, or some other negative factor. On the other hand, if the hematogenous constituents are distinctly increased beyond normal limits, the retention of excrementitious materials in abnormally large amounts clearly indicates perversion of metabolism or diminished renal permeability. For convenience, the urea nitrogen may be taken as a fairly reliable guide in the majority of instances. If this is found in excess of 20 mg., the prognosis is proportionately serious, except in cases of chronic parenchymatous nephritis, in which the nitrogenous retention is often low.

Phenolsulphonephthalein Test.—This test, which is probably as accurate and delicate as any for the determination of the functional activity of the kidneys, was introduced by Rountree and Geraghty, and at the present time is the most popular and widely used of all. The solution is prepared as follows: 0.6 gm. of phenolsulphonephthalein and 0.84 c.c. of a $\frac{2}{N}$ NaOH solution (8 per cent) are added to sufficient 0.75 per cent NaCl solution to make 100 c.c. Each c.c. of this solution represents six milligrams of the dye. The preparation, when ready for injection, is a monosodium salt, which is red in color and slightly irritating locally. Hence, two or three drops more of a $\frac{2}{N}$ NaOH solution may be added until the color is changed to a Bordeaux red, when it becomes non-irritating. The dose is one cubic centimeter. Ampules of this preparation, ready for use, can now be purchased in the market, but these usually contain more than 1 c.c. Caution must therefore be exercised to inject 1 c.c. only, and not the entire contents of the ampule.

The technic is the following: Twenty or thirty minutes before applying the test the patient is directed to drink 300 to 500 c.c. of water, to insure a free urinary secretion. Otherwise, delayed time of excretion may be due to lack of secretion. Under aseptic precautions a catheter is passed and the bladder completely emptied. One cubic centimeter of the solution (0.006 gm. of phenolsulphonephthalein) is injected intramuscularly or intravenously, the latter method being preferred, and the time noted. The end of the catheter, which has been left in situ, is placed in a test tube containing a drop of 25 per cent NaOH solution, and the time of appearance of the first pinkish tinge noted. The catheter is then withdrawn and the patient directed to rest. If the dye has been injected intravenously, the contents of the bladder are collected at the end of half an hour, either by catheter or voiding, preferably the former. If intramuscularly, the urine is collected at the end of one hour, and again in another receptacle at the end of the second hour. In prostatic or other cases where there is urinary obstruction, it is best to leave the first catheter in place continuously until the end of the observation, it being closed at the time of the first appearance of the drug in the urine until it is necessary to empty the bladder for the collection of the specimen to be tested.

The half hour, or each hour, specimen is then carefully measured, the specific gravity taken, and the urea may be estimated if desired. It is then diluted with water to 200 c.c., and 10 c.c. of a 5 per cent solution of NaOH added, which makes the urine decidedly alkaline and brings out the purple-red color. It is again further diluted to 1000 c.c., and a small quantity placed in the cup of a Duboscq, Sargent, or Hellige colorimeter, for comparison with the standard solution in the other cup.* Readings are then taken to estimate accurately the percentage amount of the drug eliminated. The color is not affected by the ordinary urinary pigments nor by pus.

In normal cases it has been found that the time of the first appearance of phenolsulphonephthalein in the urine after intramuscular injection is from 6 to 11 minutes, and that 35 to 60 per cent is eliminated in the first hour, and 20 to 25 per cent additional in the second hour (60 to 85 per cent in all). From these figures it is apparent that the limit of error allowed for normal cases is about 25 per cent, which is entirely too wide a latitude. When intravenous injection is practiced, the first appearance of the dye occurs in from 4 to 6 minutes, and 30 to 40 per cent is excreted by the kidneys in half an hour, in normal cases. These figures are far more reliable.

The elimination of the drug does not necessarily run parallel to the excretion of water. The smaller the amount of water in normal cases, the greater the concentration of the dye. It is immaterial, however, so far as the excretion of the drug is concerned, whether the urinary output is 50 or 400 or more cubic centimeters.

The phenolsulphonephthalein test, performed in this manner, can be utilized by the general practitioner, and no special instruments other than a colorimeter are required. He can thus determine in general the metabolic capabilities of his patient and gain a reasonably definite idea of the renal efficiency. It is important to remember that

* The Duboscq and Sargent colorimeters are expensive, while the Hellige is comparatively inexpensive, and gives very satisfactory results. Utmost accuracy, simplicity and rapidity of the test are claimed for this instrument.

allowance must always be made for possible unilateral disease with compensatory hyperactivity of the other kidney, the sum total of which may closely approximate the normal. The absolute amount of work, as well as the relative proportion, done by each kidney can be ascertained by obtaining the urine from each kidney separately. To differentiate the two sides, not only is the use of a cystoscope necessary, but a ureteral catheterizing instrument is required, so that the urine may be collected from each side and the phenolsulphonephthalein content of the specimens estimated. The normal for one side is of course one half the normal for both.

In pathological cases the renal permeability for this drug is lowered, the decrease varying in direct proportion to the extent and intensity of the disease. The greater the impairment of function, the greater will be the delay in the onset of excretion, and the less will be the quantity eliminated.

The advantages of the phenolsulphonephthalein test are the simplicity of technic, the non-toxic and non-irritating properties of the drug, the complete elimination by the kidneys, the fact that no instruments of precision other than a colorimeter are necessary, and the colorimetric method permits of fairly accurate quantitative observations. Its disadvantages are that the differentiation of the two sides requires the use of a catheterizing cystoscope, ureteral catheters, and a trained cystoscopist. Many cases of acute inflammation, ureteral stricture, etc., will be encountered where ureteral catheterism is not feasible, even if available. It also often inhibits renal function, thereby influencing the test.

INDIGO-CARMINE TEST.—Many surgeons regard this test as superior to the phenolsulphonephthalein for the diagnosis of surgical lesions of the kidney, since a difference in excretion on the two sides is recognized more easily. It is often referred to as chromo-cystoscopy because, as the test is usually performed, conclusions are drawn from cystoscopic visualization of the ejection of colored urine from the ureteric orifices. Whereas in the phenolsulphonephthalein test the percentage excreted within a given time is taken as the index of renal efficiency, after indigo-carmine injection the time of its first appearance, the intensity of the color, and the force and character of the ejected streams, as observed through the cystoscope, are considered more significant. Practically the same knowledge can be acquired with a simple examining cystoscope in a few minutes in this manner that would require bilateral ureteral catheterization and a longer period of waiting after phenolsulphonephthalein injection.

The technic is the following: 0.04 gm. of indigo-carmine, in either powder or tablet form, is dissolved in 10 c.c. of freshly distilled water, which makes a 0.4 per cent solution. This is injected intravenously, and the time noted. The normal kidney will excrete highly blue colored urine in from 3 to 6 minutes. The ejection may commence in less time than this, which indicates especially good renal function. In the experience of the writer, the shortest time within which the dye made its appearance was 1 minute and 20 seconds. Immediately following the indigo-carmine injection the cystoscope is introduced into the distended bladder and the ureteric orifices carefully watched. As a rule, the ejection appears as a forcible dark blue jet, but in some cases of disease the traces of color may be faint or the urine may dribble from the ureteric opening. The following phenomena are suggestive but by no means positive:

Synchronous bilateral delay suggests parenchymatous or interstitial nephritis.

Marked delay on one side, with unusually early elimination from the other, indicates disease in the first instance and compensatory hyperactivity in the second.

Elimination beginning on one side from 8 to 12 minutes after the intravenous injection, although within normal time limits from the other, suggests chronic pyelitis on the side delayed.

Elimination not beginning until from 12 to 18 minutes is indication of partial ureteral obstruction or moderate impairment of renal function.

If after 20 minutes observation no ejection of indigo-carmine is noted, practically complete ureteral obstruction or serious disease of the kidney or ureter may be safely assumed.

Dribbling instead of spurting from the ureteric orifice means loss of tissue tone or partial obstruction of ureter or renal pelvis.

The advantages of this test are the simplicity of technic, the rapidity with which the results may be obtained, the easy differentiation of the two sides without the possible inhibition of renal function sometimes occasioned by ureteral catheterism, and the fact that no colorimeter is necessary. Its sole disadvantages are that cystoscopy is essential, and it does not estimate the patient's metabolic capabilities as well as the phenolsulphonephthalein. Frequently, however, the two tests may be combined to advantage. For example, in unilateral renal tuberculosis the indigo-carmine will quickly demonstrate which kidney is affected and the compensatory hyperactivity of the other, if such hyperactivity exists. To ascertain more exactly the patient's ability to tolerate proposed operative procedures, a phenolsulphonephthalein test may then be done. If the percentage of phenolsulphonephthalein is decidedly below normal, the surgeon is thus forewarned.

The urine may be collected at the end of certain periods of time after indigo-carmine injection and the percentage eliminated estimated by means of a colorimeter, as in the phenolsulphonephthalein test, but for quantitative determination this method offers no advantages over the phenolsulphonephthalein and is not quite as reliable.

PHLORIDZIN TEST.—After the subcutaneous injection of 1 to 5 cgm. of phloridzin, a glucosid sugar will appear in the urine in from 15 to 30 minutes, and continue for 2 or 3 hours. As some observers state that the excretion is never uniform, even in health, the results may be decidedly misleading when the test is performed in this manner. This method has now been superseded by the following improved technic:

A tablet consisting of 0.01 gm. phloridzin and 0.02 gm. NaCl is placed in the barrel of an all glass Luer syringe, the syringe and needle are assembled, and 2 c.c. of hot distilled water drawn up into the syringe. Solution of the tablet is effected by shaking, and when complete, the intravenous injection is made immediately. The details of this technic are important, since phloridzin is but sparingly soluble in cold water, although freely so in hot. It also rapidly crystallizes out on cooling of the solution, hence the injection must be made without loss of time. This injection of 2 c.c. of 0.5 per cent phloridzin insures a satisfactory duration and intensity of induced glycosuria, and is free from danger and untoward sequelæ.

To determine the total renal permeability, the bladder is catheterized and several test tubes are prepared, each containing a few cubic centimeters of heated Fehling's solution. The catheter is left in situ and the intravenous injection given. In three minutes urine is permitted to flow from the catheter into one of the test tubes containing Fehling's solution, and each two minutes thereafter into other test tubes similarly prepared, until typical sugar reaction takes place. When the renal function is normal, sugar appears in from 4 to 7 minutes. If no glycosuria occurs until 15 minutes or more have elapsed, impairment of renal function is indicated. The delay increases in direct proportion to the advancement of destruction of kidney parenchyma. The sugar reaction usually reaches its acme during the first 15 minutes, is somewhat reduced during the next 15 minute period, and becomes very low or disappears soon thereafter.

To differentiate the two sides, both ureters are catheterized before the phloridzin intravenous injection, and the urine is collected in separate test tubes containing Fehling's solution. Observations may be repeated on each side every 2 minutes, as before.

Occasionally in pathologic cases the glycosuria may persist for an unusually long period. Some clinicians have endeavored to determine the percentage and absolute quantity of sugar excreted, but such quantitative estimations under these circumstances are unreliable and of little practical value. In general, it may be said that delayed appearance of phloridzin sugar is rarely observed in healthy individuals, while pronounced delay of excretion denotes impairment of renal efficiency.

This test offers no striking advantages over the phenolsulphonephthalein and indigo-carmine tests, for there is nothing that can be learned from the intravenous injection of phloridzin that cannot be ascertained more easily and with less trouble by one of the other methods. Its evident disadvantages are the limited solubility of phloridzin, its tendency to precipitate on cooling of the solution, and the cumbersome technic that is necessary. Notwithstanding these facts, this test has a certain number of enthusiastic adherents among urologists at the present time.

METHYLENE BLUE TEST.—This is the oldest of all the dye tests and was formerly somewhat extensively employed by foreign observers. It never became popular in this country, probably because of its manifest unreliability. The latter may have been due in part to the fact that the drug was always injected subcutaneously or intramuscularly, and before the importance of intravenous technic was acknowledged it had been supplanted by other tests.

When 0.5 gm. of methylene blue is injected subcutaneously or into the gluteal muscles, the substance appears in the urine partly in its original character and partly in the form of a colorless chromogen, which may be converted into the pigment by adding acetic acid and heating. The dye usually appears in the urine in about 30 minutes, but both the time of onset of excretion and the amount eliminated may vary considerably in normal kidneys. It reaches its maximum in about 4 hours, and continues to be eliminated for a number of hours thereafter. The observations to be taken into account are the time of the first appearance of color in the urine, the intensity of the pigment, and the duration of elimination. If the kidneys are diseased, the excretion of methylene blue is delayed, sometimes for 2 hours or longer. This retardation is not nearly as marked in chronic parenchymatous as in chronic interstitial nephritis. The color may be estimated by the colorimetric method, but this test is by no means exact.

The sole advantage of the methylene blue test is that instruments of precision are unnecessary. Its disadvantages are numerous: the physical properties of methylene blue are partly altered in the body before it is eliminated, it requires a comparatively long time for complete excretion, the rate of excretion is often irregular, and quantitative estimation or differentiation of the two sides unduly prolongs the examination.

CRYOSCOPY.—The physio-chemical procedure of determining the freezing point of a solution, such as the urine and blood, is based upon the observations of Raoult that the freezing point varies in inverse proportion to the number of molecules it contains. The molecular weight is of no consequence in estimating the alteration, which corresponds to the number of molecules it comprises. The greater the number of molecules, the lower the freezing point. Electrolytes, however, depress according to the number of ions; they therefore cause a much greater depression than non-conducting substances. The freezing point, or cryoscopic index, of a solution is often designated by the Greek symbol Δ, and is compared with that of distilled water, which freezes at 0° C. The freezing point of normal 24-hour urine varies from $-0.9°$ C. to $-2.6°$ C. The freezing point of normal blood is fairly constant, being $-0.56°$ C. to $-0.58°$ C., although it may be reduced independently of renal insufficiency in some cases of typhoid fever, diabetes, and other conditions. If there is a pathologic process of the kidneys, interfering with their proper functional activity, the freezing point of the urine rises, because the total number of molecules is diminished. At the same time the freezing point of the blood is correspondingly lowered, because of the higher molecular concentration produced by the retention of excrementitious products. Cryoscopy of the blood is of value in determining the absolute or total renal function, especially when estimation of the relative function of the two kidneys through ureter catheterization is contraindicated, and at the present time is deemed far superior to urine cryoscopy, since its application does not disturb the urinary apparatus. In cryoscopy of the urine the renal secretion must be measured for a certain period of time, so that allowances may be made for reflex polyuria and other causes of disturbance of urinary output. Blood cryoscopy is probably the most valuable and reliable function test in determining the prognosis in chronic nephritis, and for this purpose it should be widely used. It possesses no peculiar virtues, however, in the diagnosis of surgical lesions of the kidneys. Cryoscopy of the urine has now been practically discarded as a prognostic factor, probably because it is quite evident that the retention of excrementitious material in the blood is of more consequence and clinical significance than the estimation of what is excreted through the kidneys. But it may be used as corroborative evidence when other methods are also employed. If the cryoscopic index of the blood is much below −0.60° C., nephrectomy is contraindicated, as the patient is likely to die from uremia. Paradoxical as it may seem, in many cases of existing uremia the freezing point of the blood is not lowered. This may be explained by hydremia or the albuminoid character of the uremic toxin.

The apparatus most frequently employed for freezing point determinations is Beckmann's cryoscope, although a number of modifications have been described. It consists of a flat bottomed glass cylinder for the blood, urine, or other fluid to be tested, into which dips the bulb of a very delicate thermometer, graduated to one-one-hundredth of a degree. The thermometer is rigidly suspended in its proper position, its bulb touching only the fluid in which it is immersed, and enters the cylinder through a perforated rubber stopper. A platinum wire, intended for stirring the material so that it will be of equal temperature throughout, is also introduced through another hole in the same stopper. Outside of the first glass cylinder is a second one, containing alcohol or glycerine, which is pressed down into a large glass jar containing the freezing mixture of salt and ice. Ten to twenty cubic centimeters of distilled water are placed in the first glass cylinder and continuously and regularly stirred. At the same time the freezing mixture is stirred with a heavy wire. The distilled water gradually cools and as it approaches the freezing point, the mercury in the thermometer falls rapidly. Then it stops, and suddenly rises to a high point, where it hesitates momentarily. This is the true freezing point of the distilled water under the existing physical conditions. After the freezing point of the distilled water has been taken, the water is decanted and replaced with the fluid to be tested. The entire technic is repeated and the freezing point again noted. The difference between the freezing point of distilled water and that of the fluid tested will be the index of its molecular concentration, or freezing point.

In testing blood or urine, 10 to 20 c.c. should be used. The blood is obtained by venous aspiration and may be used whole or as defibrinated plasma. The urine is best taken from a 24-hour specimen.

Experimental Polyuria.—This test was introduced by Albarran and is based on an estimation of the renal functional activity as compared with the amount and quality of the urine excreted. The urea content, freezing point, and microscopical features are emphasized. After preliminary fasting, the patient is given a pint of mineral water to drink, ureteral catheters are passed, and three separate specimens are collected from each side at the end of half an hour, one hour, and an hour and a half. There are so many possible sources of error that the conclusions drawn from the observations made are extremely indefinite.

Electric Conductivity of the Urine.—This method is a complicated procedure and of very slight practical value. It is based upon the fact that the power of a solution to conduct a current varies with its molecular concentration.

Toxicity Test.—In health, urine is poisonous when injected into rabbits and other animals, although its toxicity varies even under normal conditions. In the process of disease, its toxic content may be increased or diminished. In fevers, such as the exanthemata, it is usually increased, while in nephritis it is diminished, and the urine is claimed to be non-poisonous when the renal lesion is extensive. The practical value of this test is insignificant.

All these function tests are quite free from unpleasant sequelæ and serious complications. Catheterization of ureters, however, is not an innocuous procedure, especially if the catheters are left in situ for any considerable length of time, for it may cause a temporary hematuria, and occasionally precipitates a renal colic. When specimens are collected through ureteral catheters for quantitative estimations, the catheters should be of sufficient size to effectively plug the ureters. Otherwise leakage of urine may occur along the catheter, thus admitting a source of error. The quantity of urine, its cryoscopic index, the amount of urea, and one of the dye tests may be combined in a single examination. But as the color tests interfere with the excretion of sugar, the phloridzin test should not be done at the same time. The chief value of these functional tests is diagnostic. In addition to determining the renal efficiency in derangements of metabolism and diseases of the uro-genital tract, they also serve to differentiate an extra-renal mass from one that exists in the kidney, and will often demonstrate whether or not conditions of coma are renal in origin. While one or more function tests alone may not permit of correct judgment in any particular case, they are often of great assistance in completing the clinical picture.

APPENDIX.

WHEN many urine examinations are made, it is a good plan to have a printed blank for such examinations, which, or a copy of which, is filed away for future reference. As in the great majority of cases only the more important chemical tests are necessary, these alone should be incorporated in the blank, leaving space for any special examination to be made in certain cases. The following blank can be used for all purposes:

REPORT ON EXAMINATION OF URINE.

Patient...
From Dr...
Received..
Examined..

Physical and Chemical Examination.

Passed..
Total in twenty-four hours..........................
Reaction..
Color...
Odor..
Sediment..
Specific gravity....................................
Urea..
Urates..
Phosphates..
Sulphates...
Chlorides...
Carbonates..
Albumin...
Sugar...
Acetone...
Diacetic acid.......................................
Bile..
Indican...
Blood...
Other chemical elements.............................
Total solids..

Microscopical Examination.

Crystalline and amorphous sediments.................

Red blood-corpuscles................................
Pus-corpuscles......................................

Epithelia:
- Convoluted tubules of kidney.........................
- Straight collecting tubules of kidney...................
- Pelvis of kidney.................................
- Ureter..
- Bladder...

- Urethra...
- Prostate ....
- Seminal vesicles................................
- Vagina..
- Other epithelia..................................

Tube casts...

Pseudo-casts...
Connective-tissue shreds............................
Mucus...
Micro-organisms.....................................
Spermatozoa...
Other features.......................................

Diagnosis..

Remarks..

In filling out the blank the numbers of the different microscopical elements should be stated, and the following terms may be used:

None.
Very few.
Few.
Few to moderate.
Moderate.
Fairly numerous.
Numerous.
Very numerous.

Whenever albumin and sugar are present, the approximate percentage amounts should, if possible, be stated. When this cannot be done, the following terms, especially for albumin, may be used:

Faint trace.
Trace.
More than trace.
Small amount.
Moderate amount.
Large amount.
Very large amount.

These terms may also be employed to determine the amounts of bile and other chemical elements. For indican and acetone the terms slight excess; slight to moderate excess; moderate excess and heavy excess are indicated.

Lists of Apparatus and Reagents Required for Urinary Analysis.

In the ordinary chemical and microscopical examination of urine the apparatus and reagents required are not numerous, though they vary with the character and extent of the examinations desired. In the following lists all apparatus and reagents mentioned in the preceding pages are enumerated, many, however, being required only for more or less detailed work, such as is not carried out in routine analyses by practitioners, but only in more completely equipped laboratories. The more important ones in the first two lists are enumerated first. It is easy for the individual worker to select those required by him from these lists.

APPARATUS.

Microscope with three lenses and two eyepieces, giving a magnifying power of between 50 and 1,000 diameters.

Centrifuge, either hand, water power or electric.

Centrifuge tubes, graduated and non-graduated.

Alcohol lamp.

Asbestos filtering fibre.

Camel's hair brushes, small.

Conical glasses.

Cover glasses and slides.

Cover glass forceps.

Doremus' Ureometer or Hinds' modification.

Droppers with rubber nipples.

Dropping bottles.

Einhorn's Saccharometer.

Esbach's Albuminometer.

Filter paper.

Glass or porcelain dishes, small.

Glass funnels, different sizes.

Glass graduates, 5, 10, 25, 50, 100, 500, and 1,000 c.c.

Glass pipettes, plain and graduated, the latter 5, 10, 25, and 50 c.c.

Glass rods.

Litmus paper, blue and red.

Platinum rods, wire in glass handle.

Reagent bottles with glass stoppers, various sizes.

Ruhemann's Uricometer.

Scale with weights.

Sedimentation glass or Spaeth's sedimentation glass.

Test tubes, two or three dozen.

Test tube brushes with sponge end.

Test tube holder.

Test tube rack.
Teasing needles and spatulas.
Urinometer, preferably Squibb's.
Urinometer tube with fluted contours.
Washing bottle.
Watch glasses.

Beakers, thin glass.
Bunsen burner with tubing.
Burettes, 50 c.c. each, graduated in tenths of a cubic centimetre.
Colorimeter, Duboscq, Sargent or Hellige.
Distilling flasks.
Erlenmeyer flasks.
Filter and burette stand.
Flasks, plain, 250 and 500 c.c.
Horismascope.
Incubator.
Mohr-Westphal balance.
Polariscope.
Porcelain evaporating dishes.
Saxe's Urinopyknometer.
Thermometers.
Tripods.
Water bath, copper, fitted with rings.

LIQUID REAGENTS.

Acid, Acetic, c.p.
Acetic, glacial.
Carbolic, 5 per cent solution.
Hydrochloric, c.p., also 2 or 3 per cent solution in 95 per cent alcohol.
Nitric, c.p., also 25 per cent aqueous solution.
Phosphoric, 3 per cent solution.
Sulphuric, 20 per cent solution.
Aether, sulphuric.
Alcohol, 60 per cent, 95 per cent and absolute.
Ammonia water, dilute.
Ammonium chloride, sat. sol.
Barium chloride solution (Barium chlo. 4, HCl 1, Distilled water, 16).
Barium chloride, standard solution (Cryst. Barium chlo. 30.54, Distilled water, 1,000).
Benedict's solutions, for glucose.
Bromine, pure.
Bromine, Rice's solution (Bromine, 30, Potass. bromid, 30, Distilled water, 240).
Carbon disulphide.
Chloroform.
Cochineal tincture.
Distilled water.
Esbach's solution (Picric acid, 1, Citric acid, 2, Distilled water, 100).
Fehling's solutions (Copper sulphate, and alkaline tartrate).

Ferric chloride, 10 per cent solution.

Glycerine.

Gram's solution (Iodine, 1, Potassium iodide, 2, Distilled water, 300).

Hydrogen peroxide.

Magnesian fluid (Magnesium sulphate, 1, Ammonium chloride, 1, Distilled water, 8, Ammonia water, 1).

Magnesium sulphate, sat. solution.

Nitrate of silver solution (1 to 8).

Nitrate of silver, standard solution (29.075 fused silver nitrate, Distilled water, 1,000).

Obermayer's reagent (HCl, c.p., 500, Ferric chloride, 1).

Potassium chromate, neutral, sat. aqueous solution.

Potassium ferrocyanide, 5 and 10 per cent and saturated solutions.

Potassium hydroxide, 10 per cent and sat. solutions.

Potassium nitrite, 1 per cent solution.

Potassium permanganate, 0.5 per cent solution.

Potassium sulphate solution (Pot. sul. 21.778, Distilled water, 1,000).

Ruhemann's Iodine solution (Iodine, 0.5, Potassium iodide, 1.25, Absolute alcohol, 7.5, Glycerine, 5, Distilled water, q.s., 100).

Sodium acetate solution (Sod. acet. 100, Distilled water, 900, then add 30 per cent acetic acid sol. 100).

Sodium hydroxide, 10 per cent and sat. solutions.

Sodium hydroxide, 100 to 250 distilled water.

Uranium nitrate, 5 per cent solution.

Uranium nitrate or acetate, standard solution (35.5 of the salt to 1,000 distilled water).

Acid, Boric, c.p.
- Hydrochloric, decinormal solution.
- Nitrous, c.p.
- Picric, 10 per cent and saturated solutions.
- Phosphotungstic, 10 per cent solution.
- Sulpho-salicylic, 20 per cent and saturated solutions.

Amyl alcohol.

Ammonium hydroxide.

Ammonium sulphate, saturated solution.

Anilin oil.

Copper sulphate, 10 per cent solution.

Diazo reagent (Sulphanilic acid 0.1, HCl 5, Distilled water 100).

Formaldehyde, 40 per cent solution.

Haines' solution (Copper sulph. 2, Distilled water, 16, Glycerine, 16, Pot. Hydr. 160).

Haines' solution, modified (Copper sulph. 5, Glycerine, 280, Pot. Hydr. 20, Distilled water to 1,000).

Lead acetate, 20 per cent solution.

Lugol's solution (see Gram's solution).

Methyl orange, 0.5 per cent solution.

Oil of turpentine.

Sodium acetate, 40 per cent solution.
- carbonate, 0.25 per cent solution.

Sodium chloride, sat. solution.
hydroxide, decinormal solution (4 gm. in litre).
nitrite, 0.5 per cent aqueous solution.

Spiegler's reagent (Mercuric chloride, 10, Succinic acid, 20, Sod. chlor. 20, Distilled water, 500).

Thymol, 10 per cent alcoholic solution.

Tincture of Guaiacum.

Tincture of Iodine.

Toluene.

Zinc chloride, 5 per cent alcoholic solution.

Staining Reagents for Bacteria.

Bismarck brown, 1 or 2 per cent aqueous solution.

Fuchsin, carbolic acid solution (Fuchsin, 1, Absolute alcohol, 10, Carbolic acid, 5 per cent aqueous sol. 90).

Gentian violet solution (Con. alcoh. gent. violet sol. 10, Carbolic acid, 5 per cent aqueous sol. 90).

Methylene blue solution (Con. alcoh. methyl blue sol. 30, 0.01 per cent caustic potash 100).

Solid Reagents.

Acid, Boric.
Acid, Citric.
Acid, Picric.
Acid, Succinic.
Ammonium chloride.
Ammonium sulphate.
Bismarck brown.
Bismuth subnitrate.
Calcium hypochlorite.
Chromic acid.
Copper sulphate.
Ferric chloride.
Fuchsin.
Gentian violet.
Indigo-carmine.
Lead acetate.
Lead acetate, tribasic.
Lead carbonate, powdered.
Magnesium sulphate.
Mercuric chloride.
Mercuric chromate.
Methylene blue.
Orcin.
Para-amido-aceto-phenone.
Phenolsulphonephthalein.
Phenylhydrazin hydrochlorate.
Phloridzin.
Phosphotungstic acid, crystalline.
Potassium bromate.
Potassium chlorate.
Potassium chromate.
Potassium ferrocyanide.
Potassium hydroxide.
Potassium iodide.
Potassium nitrite.
Potassium oxalate.
Potassium permanganate.
Resorcin.
Sodium acetate.
Sodium carbonate.
Sodium chloride.
Sodium hydroxide.
Sodium nitro-prusside.
Sodium nitrite.
Sulphanilic acid.
Sulpho-salicylic acid.
Thymol.
Urease.

LANE MEDICAL LIBRARY

To avoid fine, this book should be returned on
or before the date last stamped below.

NOV 20 1953

1500

J53 Heitzmann, L. 97172
H47 Urinary analysis.
1921

NAME	DATE DUE
Charles King / Eileen King	NOV 20 1983

9-41-3M