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LAWRENCE WOLFF, M. D.

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THE

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CHEMICAL AND MICROSCOPICAL,

FOR

CLINICAL PURPOSES.

ARRANGED IN THE FORM OF

QUESTIONS AND ANSWERS.

BY

LAWRENCE WOLFF, M.D.,

PHYSICIAN TO THE GERMAN HOSPITAL OF PHILADELPHIA; DEMONSTRATOR OF CHEMISTRY,
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PREFACE.

The favorable reception accorded to my little book on "The Essentials of Medical Chemistry," together with a wish expressed by many of its readers that it should also contain a special part on urinology and urinalysis, have caused the preparation of this little volume on "The Examination of Urine, Chemical and Microscopical, for Clinical Purposes."

As its scope has a more clinical than purely chemical bearing, it was thought best to present it in separate form rather than as part of a work on medical chemistry. It is intended as an aid for the student in his *studies* on this subject, more so than as a manual for his laboratory practice in chemistry.

The author trusts that as such it will be a welcome friend to the student and help him to master the essentials of this branch of medical science, which is of such great importance in the study of disease.

L. W.

Philadelphia, Pa.,
333 South Twelfth St.,
February, 1890.

LIST OF ILLUSTRATIONS.

TABLE OF CONTENTS.

THE EXAMINATION OF THE URINE.

Which are the objective points in the examination of urine for clinical purposes?

The quantity, appearance, color, odor, reaction, specific gravity, increase or decrease of normal ingredients and presence or absence of abnormal or adventitious substances.

When should the specimen be obtained for examination?

For qualitative purposes the specimen may be taken at any time of the day, the morning urine in preference. For quantitative examination a specimen of the total urine in 24 hours must be used.

How is the total urine of the 24 hours to be collected?

The urine passed at a certain hour is to be thrown away, all subsequently passed up to the same hour of the next day is to be collected in a clean glass jar or bottle and the amount measured.

How soon thereafter should the urine be examined, and why?

Shortly after the specimen is obtained, as putrescence will rapidly set in, which will change the character of some of the ingredients.

What is the average daily quantity voided under normal conditions?

1200 to 1500 c.c., or about 40–50 fluidounces.

Under which normal conditions is this increased or diminished?

Copious drinking increases the quantity; also, a lower temperature or great humidity of the atmosphere; free sweating, purgation or emesis will diminish it.

Which pathological conditions increase the quantity and which diminish it?

Diabetes insipidus and diabetes mellitus largely increase the quantity, acute febrile affections diminish it. It is also increased in certain nervous affections and diminished in hydropic conditions and some renal diseases.

In which way is the appearance of the urine to be noted?

If clear, turbid, or containing a sediment.

Which are the principal causes of turbidity or sedimentation in the urine?

The presence of mucus, precipitation of the earthy phosphates from alkaline reaction, separation of urates by lower temperature, and pathologically the presence of pus or fat in minute subdivision, the latter causing a layer to rise to the surface.

What is the normal color of urine, and how are the variations expressed?

The normal color of urine is yellow, the variations being expressed by Vogel's scale, which contains three yellow, three red and three brown tints, termed respectively pale yellow, light yellow, yellow, reddish-yellow, yellowish-red, red, brownish-red, reddish-brown, brownish-black. (See Frontispiece.)

Which are the normal urinary coloring bodies?

Indican and urobilin; others frequently described are modifications of the latter.

How is urobilin derived?

From the blood; the hæmoglobin changing to hæmatin, this to bilirubin, which by taking up hydrogen is changed to hydro-bilirubin, identical with urobilin.

What is indican, and how derived?

This is sometimes called uroxanthin, and is chemically potassium indoxyl-sulphate, a normal component of the urine, varying in quantities, and derived from disturbances of intestinal digestion and consequent absorption of the indol of the fæces.

How is the presence of indican in the urine demonstrated, and how determined?

Indican can be demonstrated by mixing urine with about ¼ quantity of HCl, when, upon standing 24 hours, a red, purple, or blue color will appear, which if shaken out with chloroform and the separated solution compared with a standard solution of indigo in chloroform diluted to the same tint, may be expressed in the quantity of indigo it represents.

What is the color of urine in icterus, and by what produced?

The urine in this condition is of a yellow or greenish, or even greenish-black color, caused by the presence of biliary coloring matter.

How may the presence of blood in the urine affect its color?

It will cause a change of color from light red to brown and almost black.

Do medicinal agents change the color of the urine?

Many of them do: Thus, it is turned brown or black after ingestion of carbolic acid and gallic acid, yellow after santonin, rhubarb (changed to red by addition of ammonia), also, after senna, logwood, etc.

What pathological condition gives rise to a dark brown or blackish color of urine, and why?

Melanotic tumors, owing to the elimination by the kidneys of uromelanin, a black coloring body corresponding to the choroidal pigment.

Describe the odor of fresh normal urine.

Fresh normal urine has a specific, not disagreeable, aromatic odor, due to the organic acids of the aromatic series.

How does this change on standing?

The urine turns alkaline in reaction, and then ammoniacal decomposition takes place, giving rise to a disagreeable ammoniacal odor. This may take place already within the bladder in cystitis.

In what conditions and by which medicines or food is the odor of the urine modified?

In diabetes the urine has often a fruity odor, due to acetone. Asparagus gives it a disagreeable odor. Spirits of turpentine an odor not unlike violets. Copaiba, cubebs, balsam of tolu and oil of sandalwood give it an aromatic odor.

What is the effect of mineral acids, and what of fixed alkalies on the normal odor of the urine?

Mineral acids interfere with the normal odor, fixed alkalies make it aromatic.

Has the urine containing blood a special odor?

It has a slightly putrid odor, resembling that of high game.

What is the reaction of normal urine? What due to?

It is normally slightly acid, due to the presence of acid sodium phosphate. The acid reaction is greatest in the urine of the night, less in that voided after meals.

How is the reaction of the urine ascertained?

If blue litmus paper is touched with a drop of acid urine it will be turned to a red color; if the urine is alkaline, it will turn red litmus paper blue. If, upon exposure in the latter case until dry the red color is restored, this alkalinity is due to ammonia.

In which way is the degree of acidity of urine determined?

By acidimetry, *i. e.*, titration with a decinormal solution of potassium hydrate, expressing the result in the corresponding amount of oxalic acid.

What is the relation of the acidity of urine to disease?

Many diseases show a direct relation with it. Thus, in typhoid fever the acidity is in direct ratio with the fever, in rheumatism with the pain, while in pneumonia, pleurisy, emphysema, etc., the urine is very acid.

Which systemic conditions may cause an alkaline reaction of the urine?

Fear, nervous affections, etc., may bring about alkalinity. Irrespective of food, it is associated with anæmia, debility, etc. This alkalinity is due to fixed alkalies.

Under what local conditions may the urine become alkaline?

In cystitis the urea is decomposed into ammonium carbonate, which renders it alkaline, with ammoniacal odor.

What effect has the alkaline reaction on the urine?

The alkalinity from fixed alkalies causes the precipitation of the earthy phosphates, rendering it of white color. Ammoniacal alkalescence brings about the formation of triple-phosphate.

How do medicinal agents influence the reaction of the urine?

Mineral acids do not directly influence its reaction; alkaline hydrates and carbonates render it less acid or alkaline; the salts of the vegetable acids, being eliminated as alkaline carbonates, produce alkalinity; benzoic acid or alkaline benzoates are converted into hippuric acid and increase the acidity of the urine.

What does the specific gravity of the urine represent?

The amount of solids contained in solution therein.

State the average specific gravity of normal urine and its variations under various conditions.

FIG. 1.

Urinometer.

The average specific gravity of the normal urine is between 1015 and 1025. When great quantities of liquids are ingested it may fall to 1002, and when great amounts of fluids are withdrawn it may reach as much as 1040.

In which diseases is the urine characteristically high, and in which relatively low?

In diabetes mellitus it is always high, and may reach 1050; in the various forms of Bright's disease, as well as in amyloid degeneration of the kidneys, it is low, reaching 1005 to 1004.

How is the specific gravity of urine ascertained?

With the urinometer (Fig. 1); fill the cylinder for that purpose about three-quarters full, then carefully float the urinometer in it and add enough urine to fill the cylinder to the top, reading off the degree of immersion over the top of the liquid. For very accurate determinations, the specific gravity should be taken with the specific-gravity bottle.

For what purpose does the knowledge of the specific gravity of urine serve?

For the approximate determination of the quantity of solids. Thus, if by Trapp's formula the last two figures of the specific gravity are multiplied by 2, it gives the amount of solids contained in 1000 parts; (the factor 2.33 is sometimes used as being more accurate, but 2 suffices for clinical purposes).

The Normal Constituents of Urine.

What constitutes the normal solid components of urine?

The products of retrograde metamorphosis of nitrogenous bodies, together with the inorganic matter eliminated as waste material by the kidneys from the circulation.

How are they classed according to their chemical character, and what are they respectively?

They may be classed as organic, which form the greater part, and inorganic. The principal ones of the former class are urea, uric acid, hippuric acid, kreatinin, xanthin, sarkin, oxalic acid, oxaluric acid, aromatic ethyl-sulphuric acids, sulphocyanic and succinic acids, sugar, lactic acid, pigments, and extractives. The inorganic are chlorides, phosphates and sulphates of potassium, sodium, ammonium, calcium and magnesium, iron, silicic acid, nitrites and nitrates, also hydrogen peroxide.

Are these constant in proportion, and what influences their presence in the urine?

They are subject to continuous change: thus, a more liberal animal diet increases the amount of urea; age, sex and great exertions influence their amount as well as pathological conditions.

Normal Organic Constituents of the Urine.

Which is the principal solid ingredient of the urine, and what is it?

Urea, a carbonyl diamide, often termed carbamide (CON_2H_4), the ultimate product of oxidation of the albuminoids introduced into or composing the body.

How much urea is excreted under normal conditions daily?

500 grains, or about 30 grammes, which, however, may vary according to the character of the ingested food.

How may the urea be separated and demonstrated from the urine?

By acidulating the condensed urine either with nitric or oxalic acid, and allowing the nitrate or oxalate of urea to crystallize from this.

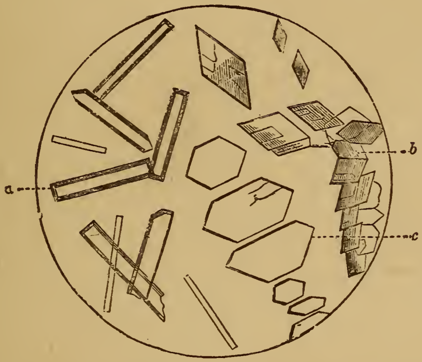
Under which pathological conditions is the elimination of urea increased?

In febrile conditions which do not suppress the renal action. Thus, it is increased in meningitis, typhoid fever, smallpox, erysipelas, intermittent fevers, pneumonia, pleurisy, articular rheumatism with endocarditis, etc.

What pathological conditions diminish the urea in urine?

A diminished nutrition, especially of albuminoids, processes of suboxidation, such as emphysema, valvular disease of the heart and disturbances of the circulation, in which the amount of urea produced is less; in other diseases, such as ascites and anasarca, the urea is not secreted, though produced, and is withheld in the circulation; also in cholera and diseases characterized by renal inaction, when with an amelioration the urea reappears. The wasting diseases, such as anæmia, leucocythæmia, phthisis, acute yellow atrophy, etc., are also accompanied by a diminished amount of urea in the urine.

FIG. 2.



a, urea; *b*, rhombic, and *c*, hexagonal plates of urea nitrate.

Can urea ever exist as a sediment in urine?

On account of its ready solubility it can never exist as such.

How can urea be recognized under the microscope?

By evaporating a drop of urine cautiously on a slide, when, with a low power, the rhombic prisms of urea may be readily recognized (Fig. 2).

How may the oxalate or nitrate of urea be prepared?

By acidulating condensed urine with either oxalic or nitric acid, when the respective oxalate or nitrate will crystallize out on cooling, in hexagonal plates (Fig. 2).

By what chemical test may urea be recognized?

By the Biuret reaction. This consists of heating a specimen of urea until it ceases to give off ammoniacal vapors; when to the residue a little potassium hydrate is added and a drop of cupric sulphate solution, the color is changed to a reddish violet.

Which are the principal agents to break up urea?

Stronger mineral acids and hydrates of the alkalies cause it to take up water and split up into carbon dioxide and ammonia. Nitrous acid splits it into carbon dioxide water and nitrogen, as do also the alkaline hypochlorites and hypobromites. Certain microörganisms also cause it to break up into ammonium carbonate.

What is Fowler's method for determining the amount of urea in urine, and how applied?

The differential density test. To apply this, the specific gravity of the urine is first accurately determined and noted and then the specific gravity of the specimen of liquor sodæ chloratæ (Labarraque's solution) to be employed. The latter is multiplied by 7 and the product added to the amount of the sp. gr. of the urine; the sum so ascertained is divided by 8, which gives the sp. gr. of a mixture of 1 part of urine and 7 parts of the hypochlorite solution. After this add 1 part urine to 7 parts of Labarraque's solution, and after standing for an hour or two, take the specific gravity of the mixture after the reaction has been completed. This specific gravity subtracted from that first computed for the mixture of the two before reaction, and the difference multiplied by 0.77 gives the percentage of urea in the urine examined.

What is Liebig's method of determining urea by titration?

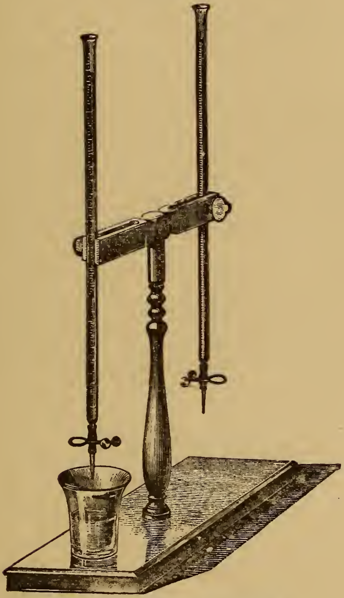
The method depending on the formation of an insoluble compound of mercuric nitrate with urea, and the computation of the amount of urea from a standardized mercuric nitrate solution used for this purpose.

Which are the reagents and apparatus used in this method?

A standardized mercuric nitrate solution, of which each c.c. is equal to 1 centigramme urea. A baryta mixture of 1 part saturated solution of barium nitrate and 2 parts cold saturated baryta water.

A saturated solution of sodium carbonate, a graduated burette, a volume pipette, watch-glasses, glass rod and beaker glass (Fig. 3).

FIG. 3.



Burette-stand and Burettes.

How are the sulphates and phosphates and carbonates first separated in this process?

By mixing 40 c.c. urine with 20 c.c. baryta mixture, after which the liquor is filtered and 15 c.c. is measured into a beaker glass; these 15 c.c. correspond to 10 c.c. urine. At times, if the urine contains an excess of phosphates or alkaline carbonates, it becomes necessary to take more baryta mixture, and then the specimen to be examined must be increased always so as to represent 10 c.c. urine.

In which manner is the titration of the urea performed, and how is the indicator applied?

The mercuric solution is dropped from the burette into the filtered urine, amidst constant stirring, until it ceases to produce a precipitate; then a few drops are taken out into a watch-glass and an equal amount of the soda solution allowed to flow into it. When the resulting reaction begins to show a yellow color, the saturation is complete, if not, more of the mercuric solution is dropped from the burette as above.

How is the result now computed?

As each c.c. of the mercuric nitrate solution is equal to 0.01 gramme urea, as many as were necessary to saturate it were contained in 10 c.c. urine, or ten times that amount constitutes the percentage of urea; from the number of c.c. of mercuric solution 2 c.c. are first to be deducted to allow for the sodium chloride which also enters into this process. Thus if 30 c.c. were used, 28 c.c. would represent 0.28 gramme urea contained in 10 c.c. urine, or 2.8 would be the percentage.

If albumin is present what has to be done first?

The urine must be faintly acidulated with acetic acid, and then the albumin, coagulated by boiling, is separated by filtration before the titration of the urine.

What are the principles of the azotimetric method for the determination of urea in urine?

The urea of the urine is decomposed by a solution of sodium hypobromite (Knop's solution), thus liberating the nitrogen of the urea while the water remains and the carbon dioxide is arrested by the alkaline test solution. The nitrogen is then corrected for temperature, atmospheric pressure and tension of aqueous vapor, and the amount of urea corresponding to each c. c. thereof is equal to 0.0027 gramme.

What comprises the most simple apparatus for this process?

A flask containing 15 c. c. hypobromite solution and also a test tube standing slantingly in it, into which 5 c. c. urine are added. The flask is connected by a rubber tube to an inverted burette or cylinder graduated into c. c.; this latter is contained in a cylinder filled with water and is immersed therein to the zero mark, so that the water in the graduated tube and the cylinder are on an equal level.

How is the Knop's solution made?

Dissolve 100 grammes sodium hydrate in 250 c.c. water and add 25 c.c. bromine.

How is the process applied?

By allowing the urine to commingle with the hypobromite solution, when the reaction will take place; as the N escapes into the graduated cylinder the latter is raised so as to keep the water inside and outside always on the same level. When the reaction is complete and no more gas given off the number of c.c. are read off.

How is the volume of N so observed corrected and how the urea computed from it?

The volume of nitrogen so observed has to be corrected for temperature, barometric pressure and tension of aqueous vapor. As 1 gramme urea yields 370 c.c. nitrogen at 0°C. and 760 mm. pressure the formula for correction of its observed volume is as follows for 100 c.c. urine:

$$U = \frac{100\ v.\ (b - b')}{760.\ 370.\ x.\ (1 + 0.00366.t)}$$

In this formula

U stands for percentage of urea to be determined.
v the volume of nitrogen read off.
b barometric pressure.
b′ tension of aqueous vapor.
x the measure of urine employed.
t the temperature (C°) at which the process is conducted.

Instead of this correction the corrected weight in milligrammes for each c.c. nitrogen may be taken from Dietrich's table by entering with barometric pressure from above and the temperature from the side, when the corrected weight will be found at the intersection of the two lines. (See Dietrich's table on last page.)

Thus if 10 c.c. N were observed at 15° C. and 740 mm. pressure, each c.c. N would weigh 1.1399 milligramme, or 10 = 11.399, which if multiplied with 2.14 would give the amount of urea in the urine used 24.39388 milligrammes, which if it had been 5 c.c. is multiplied with 20 gives the percentage = 0.49.

Does the method give absolutely correct results?

No, the theoretical amount of N is never obtained; this may be rectified by multiplying the result with 1.044, but even then it is not absolutely correct.

What modifications of the above described apparatus may be used for clinical purposes?

Such apparatus as that of Lyon, which contains on the cylinder, instead of c.c., subdivisions corresponding to the percentage of urea at a temperature of 70° F. Pressure and tension of aqueous vapor may be then neglected if the temperature is at or about 70° F.

What is uric acid?

A bibasic acid of the formula $C_5H_4N_4O_3$ which in the form of salts is a normal ingredient of the urine and next to urea the principal eliminant of nitrogen from the body; the quantity eliminated under normal conditions during 24 hours amounts from about 0.5 to 1 gramme.

Under which normal and abnormal conditions is the amount of uric acid in the urine increased or decreased?

Nitrogenous food increases and carbohydrates diminish the uric acid in the urine. In diseases of the respiratory and circulatory system, as in pneumonia, capillary bronchitis, pleuritic exudations, pericarditis, etc., the amount in the urine is increased, also in most fever processes. Chronic diseases are accompanied by a diminished amount of uric acid in the urine; it is diminished also after profuse hemorrhages and in anæmia, chlorosis, spinal and renal affections, as well as in chronic rheumatic and gouty conditions. During the exacerbations of malarial fevers there is an increase in the elimination of uric acid, as well as in typhoid fever, inflammatory rheumatism, smallpox and in septic fevers.

How is uric acid separated from urine?

By acidulating 500 grammes urine with 10 grammes hydrochloric acid, when, after standing 24 hours, the uric acid will crystallize from it all but a very small amount held in solution.

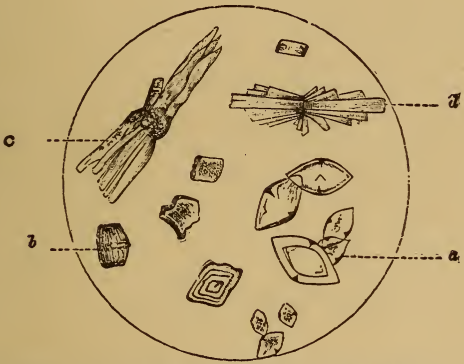
What are the physical properties and microscopical appearances of uric acid separated from urine?

Uric acid is very little soluble in water, about 1 to 18,000, insoluble in alcohol and ether, readily soluble in the neutral alkaline phosphates and carbonates. The crystals separated from the urine appear to the naked eye as small reddish-brown particles. Microscopically they present a variety of shapes which, however, may be regarded as modifications of rhombic plates. The most frequent of these are the whetstone or lozenge form rounded off at their obtuse angles; other forms resemble barrels, sheaves, rosettes, combs, etc, (Fig. 4).

Is free uric acid ever present in the urine?

It may be present in the urine under abnormal conditions at micturition, when it may give rise to the formation of urinary concretions.

FIG. 4.



a. Rhombic crystals of uric acid, of whetstone or lozenge shape. *b.* Barrel shaped. *c.* Sheaves. *d.* Rosettes of whetstone shaped crystals.

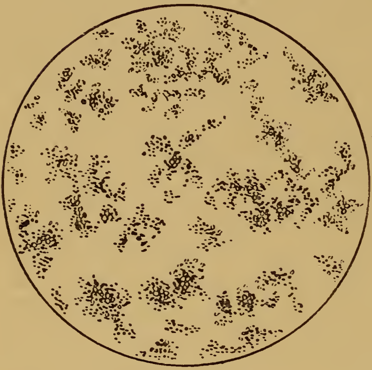
Which are the principal salts of uric acid present in the urine?

The salts of the alkalies and alkaline earths; these form both neutral and acid salts, the neutral salts being more frequent in normal urine and are more soluble than the acid salts; the acid sodium urate and potassium urate appear frequently as sediments in the acid urine of catarrhal and rheumatic affections and in fevers, and have a reddish color, owing to the presence of uroerythrin (lateritious deposits). They may be recognized by being redissolved in the urine on heating and on addition of alkaline hydrates, also by the microscope as presenting an amorphous granular appearance, as in accompanying cut (Fig. 5). The acid ammonium urate is often found in alkaline urine together with triple phosphate and presents the shape of yellow spheres with one or more hooklets attached, often occurring in attached pairs (Fig. 6). Ammonium urate is present in some vesical concretions and when preformed in the bladder may be the cause thereof.

By which test may the presence of uric acid be shown, and how is it applied?

By the murexide test; this consists in dissolving in an evaporating dish a small quantity of the substance to be examined in a few drops of nitric acid, and evaporating over a moderate heat to dryness. If the dry residue is touched with a drop of ammonia water or exposed to its vapors the bright purple color of murexide will appear if uric acid was present.

FIG. 5.



Acid sodium urate.

FIG. 6.

Triple phosphate and ammonium urate.

How is the amount of uric acid in urine determined?

By acidulating 200 c.c. urine with 10 c.c. HCl and setting it aside for 48 hours. The crystals which have separated are now collected on a weighed filter and well washed with cold water; the filter is then dried until it ceases to lose weight, and for each 100 c.c. fluid employed 0.0038 gramme uric acid is to be added to the increase of weight over that of the empty filter, which gives approximately the amount of uric acid present.

What is hippuric acid?

A normal monobasic acid of the urine, of the formula $C_9H_9NO_3$, which may be regarded a benzoyl glycocin, as it splits up into benzoic acid and glycocin.

In what amounts is it present in the urine and under what conditions may this be increased?

About 0.5 to 2.0 grammes are excreted during 24 hours in the urine, which is increased by vegetable and diminished by animal diet. Benzoic, cinnamic and quinic acids are converted in the body into hippuric acid and excreted as such. It is said to be increased in diabetes mellitus, also in hepatic affections and in jaundice.

FIG. 7.

Hippuric acid.

State the physical properties and microscopic appearance of hippuric acid.

It is readily soluble in alcohol, less so in ether, and dissolves only in 600 parts of water; it crystallizes in colorless, long, four-sided rhombic prisms, which frequently form stellate bundles (Fig. 7).

What is kreatinin?

A constant component of the urine, of the formula $C_4H_7N_3O$, supposed to be derived from the kreatin of the muscles. About 1 gramme is daily excreted under normal conditions and mixed diet.

State its properties.

It is a basic body which, when pure, forms colorless, prismatic crystals, soluble in 11 parts of water, and readily soluble in alcohol. In alkaline solutions it changes to kreatin, which, with acids, loses H_2O, and forms again kreatinin.

Under which pathological conditions is it increased, and under which decreased?

In acute diseases, especially typhoid fever, pneumonia, etc., it is increased in quantity; in anæmia, chlorosis, marasmus, tuberculosis, and progressive muscular atrophy it is diminished.

What are xanthin and sarkin?

Extractives of the urine closely allied in chemical composition to uric acid,

$$\underset{\text{(uric acid.)}}{C_5H_4N_4O_3,} \quad \underset{\text{(xanthin.)}}{C_5H_4N_4O_2,} \quad \underset{\text{(sarkin.)}}{C_5H_4N_4O,}$$

but of no clinical interest.

Normal Inorganic Constituents of the Urine.

Which are the principal ones of these?

The chlorides, phosphates, and sulphates, which are principally derived directly from the food, but the latter two also result as oxidation products from albuminoids and other bodies which contain phosphorus and sulphur.

Name the most important inorganic salts.

The one which occurs in largest quantities is sodium chloride, next is sodium acid phosphate, also, calcium and magnesium phosphates, the sulphates of sodium and potassium, and traces of iron and silicic acid.

What is the normal amount of chlorides excreted in 24 hours, and what is their importance?

The sodium chloride, which is the principal one of them, is excreted to the amount of about 16.5 grammes in the 24 hours, varying with the quantity ingested. A considerable amount is always retained in the circulation, serving probably the purpose of cell-nutrition by facilitating the osmotic process. A surplus appears in the urine.

Under which pathological conditions are the chlorides in the urine decreased?

They decrease in all acute febrile diseases, and may, indeed, disappear altogether, to reappear with convalescence. Especially is this the case in diseases accompanied with exudations and transudations, which retain the surplus chlorides until their formation is complete. Thus we find the chlorides diminished in pneumonia, pleurisy, pericarditis, peritonitis, meningitis, also in typhoid fever and rheumatic fever. A decrease of chlorides in the urine is also marked in the nephritis accompanied with albuminuria and dropsy. During the paroxysms of malarial fever the excretion of chlorides is increased.

What are the indications for prognosis of a decrease or reappearance of the chlorides in the urine?

A considerable diminution or disappearance makes the prognosis grave, their reappearance favorable, which is again disturbed by their decrease during convalescence.

How may the chlorides in the urine be shown and their quantity be approximated?

To a specimen of urine in a test tube add a few drops of nitric acid, and then of a solution of silver nitrate sufficient until no more precipitate forms. The precipitate will be dense and curdy if the chlorides are present in normal quantities, milky if diminished, and faint if almost or entirely absent. If the bulk of the precipitate is compared with that of a normal specimen, the relative amount may be approximated.

How are the chlorides in the urine determined by volumetric analysis?

To do so accurately 10 c.c. urine are evaporated to dryness in a porcelain dish and incinerated with 2 grammes pure potassium nitrate until the charred organic matter is burned off. The residue is now dissolved in about 50 c.c. distilled water and acidulated with dilute nitric acid, the excess of which is neutralized by the addition of a little pure calcium carbonate; a few drops of neutral potassium chromate are then added as indicator.

The chlorides are now titrated with a standardized solution of silver nitrate, each c.c. of which corresponds to 0.01 gramme sodium chloride. The silver nitrate solution is added from a burette to the canary-yellow fluid until a slight change to orange shows the complete precipitation of the chlorides. For each c.c. of the former count then 0.01 NaCl, or ten times that amount, to get the percentage.

Thus, if 10 c.c. urine were used and 15 c.c. $AgNO_3$, the amount in 10 c.c. would be 0.15 grammes, or the percentage 1.5.

May the process of incineration and subsequent acidulation be dispensed with for clinical purposes?

Yes; unless the urine is alkaline, very highly colored or albuminous. If such is not the case the 10 c.c. urine should be diluted with 40 c.c. distilled water, a few drops of neutral potassium chromate added and then titrated and computed as above. As the result is generally too great, 1 c.c. is, however, deducted from the quantity of silver nitrate solution used.

In which compounds is phosphoric acid present in the urine?

As phosphates of the alkalies and alkaline earths, of which there are two-thirds of the former and one-third of the latter. The phosphates of the alkalies are principally present as sodium acid-phosphate, to which the acid reaction of normal urine is due; those of the alkaline earths as phosphates of calcium and magnesium. The total quantity of phosphoric acid normally eliminated in 24 hours is between 2 and 5 grammes.

From what is the phosphoric acid of the urine derived?

From the food and also from the retrograde metamorphosis of tissues containing phosphorus. Thus it is diminished on fasting, and increased by animal diet.

Under which pathological conditions is the phosphoric acid of the urine increased or diminished?

In the beginning of the febrile processes, the P_2O_5 is usually diminished, and decreases still more with fatal termination. With defervescence and convalescence the amount is increased, while in chronic conditions no constant relations have been established, though the earthy phosphates are no doubt increased in cerebral affections, rheumatism, osteomalacia, rachitis, whereas a decrease has been established in chronic spinal disease, renal affections and dropsy.

How can the earthy and how can the alkaline phosphates of the urine be separated?

If an alkaline hydrate, KOH or NaOH, is added to urine, and the mixture heated to the boiling-point, the earthy phosphates are thrown out and may be filtered off. If to the clear filtrate about one-third of magnesia mixture is added, the alkaline phosphates will be precipitated as ammonium-magnesium phosphate, termed triple-phosphate.

How does triple-phosphate form from ammoniacal urine in cystitis or putrid urine?

From the decomposition of urea into ammonium carbonate; this, with the magnesium phosphate, forms ammonium-magnesium phosphate.

What is the import of triple-phosphate in the urine, and what its appearance under the microscope?

Triple-phosphate, if formed in the bladder, may give rise to the formation of concretions, and as they result from ammoniacal urine, cystitis probably exists. Under the microscope, the crystals of triple-phosphate are prismatic and highly refractive, representing the form of coffin lids, after which they are named. (See Fig. 6, page 30.)

What is the deposit resulting from urine alkaline from fixed alkalies?

The earthy phosphates—*i. e.*, phosphates of calcium and magnesium—appearing under the microscope as granular masses. They have no tendency to form concretions.

How is the phosphoric acid of the urine quantitatively approximated?

By Teissier's method: Into a cylinder graduated in c.c., add 50 c.c. urine and 15 c.c. magnesia mixture; mix well and allow to settle for twenty-four hours. The total P_2O_5 will be precipitated as triple-phosphate; each c.c., by volume, represents about 0.03 per cent. of phosphoric acid, or about double that amount of phosphates.

Describe the method for the volumetric determination of phosphoric acid in urine.

This is effected with a standardized solution of uranium acetate, each c.c. of which indicates 0.005 grm. P_2O_5. To 50 c.c. filtered urine, contained in a porcelain capsule or a flask, are added 5 c.c. acidulated solution of sodium acetate (sodium acetate 10, acid acetic dil. 10, water to 100). These are heated to the boiling-point, and, while boiling, the uranium acetate solution is gradually added from a burette. When the precipitate has formed, the fluid is tested from time to time by letting a few drops run into a solution of potassium ferrocyanide. As long as no change of color occurs, the process is not finished, and more uranium solution is added. When, on testing, a reddish-brown color begins to appear, all the phosphoric acid has been precipitated. To compute the result, multiply the number of c.c. uranium solution with 0.005, which gives the P_2O_5 in 50 c.c. urine, and double that amount the percentage.

What is the quantity of sulphuric acid eliminated in 24 hours, in which form, and where derived from?

About 2 grms. are eliminated in 24 hours, partly as sulphates of the alkalies, and a small portion as organic sulpho-acids. The sulphates are derived directly by ingestion and also by elaboration in the body of sulphur into its acid.

Under which conditions are the sulphates of the urine increased, and under which diminished?

Animal diet and exertion increase the sulphates in the urine; this is also the case in acute diseases, while in chronic affections of the kidneys, they are, as a rule, diminished. Ingestion of sulphur or sulphur compounds increases the amount of sulphates in the urine.

How are the sulphates in the urine shown?

By treating urine acidulated with a few drops of nitric acid with solution of barium chloride, which will give a precipitate of barium sulphate, insoluble in water or acids.

Describe the method for determining the sulphuric acid of the urine.

This is accomplished by volumetric analysis with a standard solution of barium chloride, each c.c. of which is equal to 0.01 grm. SO_3, in the following manner :—

100 c.c. urine are acidulated with 20 drops hydrochloric acid and heated to the boiling point, when the standard barium solution is gradually dropped in from a burette until fresh additions show but a slight precipitate. This is allowed to settle, and into the clear supernatant fluid one drop added. If no further precipitate results, it must be tested for an excess of the barium chloride with one drop of a sodium sulphate solution. If this shows an excess of barium, the determination has to be made with another 100 c.c. of the same urine, using less barium solution, and thus until neither the latter nor the sodium sulphate show an excess. The standard solution contains 30.5 grms. $BaCl_2$ in 1000 c.c., and each c.c. is equal to 0.01 SO_3. Thus if 13 c.c. $BaCl_2$ was used, the percentage of SO_3 was 0.13.

Abnormal Constituents of the Urine.

What are abnormal constituents of the urine?

Bodies which are not found in normal urine and owe their presence therein to abnormal, *i. e.*, pathological conditions.

Which are the principal abnormal constituents?

Biliary pigments, biliary acids, pus, blood corpuscles, hæmoglobin, albumin, glucose, oxalic acid as calcium oxalate, cystin, leucin and tyrosin, together with certain epithelial cells and casts.

Biliary Pigments and Acids in the Urine.

How is the appearance of the urine affected by the presence of biliary coloring matter?

The color is changed to a deep yellow, yellowish green, or even brownish green and brown; it froths freely on being shaken; the froth persists longer than usual, and is of a yellowish green, or brownish color.

From which pathological conditions results the presence of biliary matters in the urine?

From icteroid conditions, which may be caused by either hepatogenous or hæmatogenous icterus. In the former, resulting from obstruction of the bile ducts, biliary coloring matter as well as biliary acids are present in the urine; in the latter, consequent upon the formation of bilirubin in the blood itself by the destruction therein of some of the red corpuscles, biliary coloring matter is found present but never biliary acids.

Which is the principal test for biliary coloring matter in the urine, and how applied?

Gmelin's test; on the addition of yellow nitric acid to some urine contained in a test tube, in a manner to cause the two to form different layers, there will be a play of colors from green, blue, violet, red, to yellow, if biliary coloring matter is present; as non-biliary urine sometimes gives off colors with this reaction, it should be closely noted that the colors appear in regular order, and that green should always form first.

What other convenient method or modification may be employed in its stead?

To mix a little urine in a test tube with an equal quantity of a saturated solution of sodium nitrate. Hold this slantingly and allow some concentrated sulphuric acid to run through the mixture and to the bottom of it, when even the smallest traces of biliary coloring matter may be detected, as above.

How may the biliary coloring matter be separated and shown?

By shaking the suspected urine with chloroform, separating the yellowish chloroform and applying the nitric acid test, as in Gmelin's method.

What other bile ingredients are at times found in icteroid urine?

Biliary acids are found in the urine of hepatogenous icterus, but never in that of the hæmatogenous variety. They are not always readily shown directly from the urine, and will then need a separation therefrom.

Which is the principal test for biliary acids, and how applied?

Pettenkofer's test. This consists in adding to some urine a small quantity of cane sugar and overlaying with this some sulphuric acid, contained in a test tube, when, if biliary acids are present, there will appear a purple zone at the junction of the two liquids. A better way is to dip a piece of filtering paper into the saccharated urine, allow this to dry and then touch it with sulphuric acid, when biliary acids will give a purple color. This test may also be made by evaporating some of the urine, with a minute quantity of cane sugar, to dryness in a porcelain dish. If a drop of sulphuric acid added thereto gives rise to purple coloration, biliary acids are present.

How is Oliver's test applied for biliary acids, and what is the composition of the reagent?

The reagent consists of 30 grains powdered meat peptone, 4 grains salicylic acid, 30 minims strong acetic acid, and water sufficient to make f℥viij. If this is added to urine containing biliary acids a turbidity will arise in proportion to the amount of acids present. This may also be shown by overlaying the urine with the reagent, when the acids give rise to a turbid zone at the junction of the two liquids.

Pyuria.

What is pyuria and its import?

Pyuria is the condition characterized by the presence of pus in the urine. It points toward the existence of an acute or chronic inflammation in the urinary tract, or the communication therewith of abscesses. The sudden appearance of large quantities of pus in the urine would point to the latter condition. Inflammatory conditions of the bladder and renal pelvis are accompanied by more or less pus in the urine. When considerable pus is present in the bladder and the urine strongly alkaline, it will form a viscid jelly, which cannot be readily evacuated.

How may pus in the urine be differentiated from mucus?

Pus is turned gelatinous and ropy by caustic alkalies, while mucus is liquefied by them with white flakes.

Which is the most definite method for detecting pus in the urine?

In the acid urine pus appears as a heavy deposit, which, if inspected under the microscope, shows the pus cells as round, opaque, granular spheres, larger than the red corpuscles; on the addition of a drop of acetic acid to the slide, the granular contents and the cell membranes disappear, and the nuclei are readily seen (Fig. 8).

FIG. 8.

Pus Corpuscles and Epithelial Cells.

By what chemical test can pus in the urine be detected?

By Donné's test. This consists in separating the settled deposit by decantation and adding to the sediment a small piece of potassium hydrate, when, upon stirring, the pus will turn a clear and tough gelatinous mass.

Chyluria.

What constitutes chyluria, and what are its causes?

The presence of fat in the urine, which gives it more or less a milky or opalescent appearance; on standing and separation the fat particles rise to the surface. It may be of parasitic origin, as in tropical countries, owing to the presence of filaria sanguinis hominis or distoma hæmatobium in the blood, the lymph and the urine. The non-parasitic form is met with occasionally in moderate climates, and its origin is attributed to degenerative changes of the kidneys.

How is the presence of fat in the urine demonstrated?

By shaking it with ether and allowing the separated ether to evaporate, when fat will be found if there has been any present. The shaking with ether will not clear up the urine entirely, as the ether will precipitate some of the albumins present in chylous urine. To thoroughly exhaust the fat in the urine, some potassium hydrate solution should be added beforehand.

Hæmaturia and Hæmoglobinuria.

What constitutes hæmaturia?

The presence of blood in the urine, as evident from the existence of intact red corpuscles therein.

In which morbid affections may blood be present in the urine?

If large quantities are present, it will most probably come from the urinary tract otherwise than the renal parenchyma. Thus inflammatory or hyperæmic conditions of the renal pelvis, ureters, also ulcerations, cancer of, or stone in the bladder, may give rise to a considerable amount of blood in the urine. If small quantities only are found present, it is more likely of renal origin, and if in addition to the blood corpuscles renal casts are found in the urine, its origin from the kidneys and the existence of parenchymatous nephritis is almost certain.

How does the blood in the urine differ in appearance according to the part of the urinary tract it is derived from?

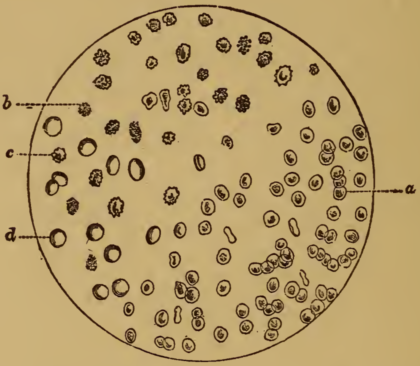
That from the renal parenchyma is well mixed with the urine and gives it a smoky appearance; if from the ureters, it is present in long semicircular clots and strings; the blood from the bladder and urethra is generally more in quantity, bright red, and settles in the urine as clots.

By which means is the existence of hæmaturia confirmed?

By the detection of the red blood corpuscles under the microscope.

To this end a small quantity of the sediment, after subsidence, is spread upon a microscopic slide with a drop of the urine, when, on inspection, the corpuscles will be brought to view in their characteristic biconcave spherical form, either single or grouped in rouleau form, or they may be crenated, as in dense urine; if they have imbibed much water, as in urine of low specific gravity, they may be swelled up and have lost their biconcavity, and they may have partly lost their contour and be partly destroyed, if the urine is ammoniacal (Fig. 9).

FIG. 9.



Blood Corpuscles.—*a*, with biconcave depressions; *b* and *c*, contracted and crenated; *d*, swollen.

What constitutes hæmoglobinuria?

The presence of hæmoglobin in the urine in a diffluent condition, and not in its corpuscular state.

How is hæmoglobinuria caused?

By a solution of the stroma of the red corpuscles in the blood leaving the diffusible hæmoglobin in solution therein which is secreted by the kidneys. The solution of the corpuscular element is noted in certain diseases, as in scurvy, typhus, pernicious malaria; also as the effect of certain poisons, such as hydrogen arsenide, phosphorus, carbolic acid, and by pressure; a periodical form is observed, the cause of which has as yet not been ascertained.

By which simple test may the presence of hæmoglobin in the urine be demonstrated?

By slightly acidulating some of the urine in a test tube with acetic acid and raising it to the boiling point. As hæmoglobin contains coagulable albumin, this will coagulate, and will, on subsiding, be found as a reddish sediment at the bottom, the soluble hæmoglobin having changed to insoluble hæmatin.

How can the hæmoglobin of the urine be demonstrated by the spectroscope?

By placing it in the light entering the prism of a spectroscope, it will give rise to two dark absorption bands in D and E of the spectrum, *i.e.*, in the yellow and in the green, the former being narrower, the latter broader.

FIG. 10.

Teichmann's Hæmin Crystals.

Which is the chemical test for hæmoglobin?

Almen's test: Add a few drops fresh tincture of guaiac to the specimen of urine contained in a test tube; after agitation add a few drops of old spirit of turpentine or ozonic ether (ethereal solution of hydrogen peroxide); if hæmoglobin is present, the color will change to a distinct blue.

In which manner may the presence of hæmoglobin be most definitely and positively established?

By the production of Teichmann's crystals of hæmatin hydrochloride, often termed hæmin. To this end the slightly acidulated urine is boiled, and the coagulum filtered off; a small portion of this is dried with a gentle heat on a microscopic slide; to the dry residue a trace of common salt (NaCl) is added and well mixed with it, and, after adding one or two drops of glacial acetic acid on the mixture, this is covered with a cover glass, and heated over a lamp to the boiling point of the acid; after cooling, and on examination under the microscope, there will be found present numerous flat, rhombic prisms or tables, of a brown or blue color, which are hæmin, or better termed hæmatin hydrochloride (Fig. 10).

Albuminuria.

Which are the albumins found in the urine of albuminuria?

Principally serum-albumin, but also, and rarer, paraglobulin.

Under which conditions may albumin appear in the urine?

When the blood is surcharged with albumin, as after excessive ingestion of albuminoids; if the blood is much diluted, when œdematous exudations will take place; when the blood pressure in the kidneys is abnormally increased; also, if the chlorides of the blood are wanting, as well as if blood or pus is admixed with the urine.

Which pathological conditions are accompanied by temporary albuminuria?

The acute febrile affections, such as typhoid fever, diphtheria, pneumonia, etc., also the exanthematous diseases during their efflorescence.

When is the presence of albumin in the urine more persistent?

In the various inflammatory affections of the kidneys, variously termed Bright's disease of the kidneys, also in heart and respiratory diseases.

What are the general appearances of albuminous urine?

As a rule it is of pale color, low specific gravity, and when shaken maintains its froth for some time.

How is urine tested for albumin by Heller's test ?

To a small quantity of urine in a test tube some nitric acid is added by allowing it to flow down the sides of the inclined test tube, so that the two fluids form separate layers ; if albumin is present there will appear at their line of contact a white zone of coagulated albumin. This may be also the result of the presence of urates, but in this case the white zone is not as distinct and more toward the surface of the urine. If warmed, the urate cloud will disappear, but not the albumin.

In which way is the boiling test performed ?

In this test the urine should be clear, and has to be filtered if turbid ; if it is neutral or alkaline it has to be made slightly acid by the addition of a drop or more of acetic acid. If the upper part of the urine in the tube is now heated to the boiling point, it will be rendered turbid if albumin is present, and may readily be contrasted with the clear layer at the bottom. If the total volume is boiled, the entire albumin therein will be coagulated, and the flocculent coagulum may be separated by filtration. Should too much acetic acid have been added, the coagulation may have been prevented by the formation of acid-albumin. This can be demonstrated and corrected by the addition of a few drops of potassium ferrocyanide solution, when the coagulum will form at once.

How can the boiling test be utilized to approximate or comparatively estimate the quantity of albumin for clinical purposes ?

By allowing the coagulated albumin of the total urine in the test tube to subside for 24 hours and expressing the volume of the coagulum in comparison with the total urine boiled, as, for instance, ¼ or ½ albuminous layer.

How can picric acid be utilized for detecting albumin in urine ?

If a concentrated solution of picric acid is added to urine there will be a coagulum formed if albumin is present. As this may, however, be caused also by alkaloids or peptones, this test can be used for the exclusion of albumin only, but if found present, it should be confirmed by either of the preceding tests.

In which way may the picric acid test be used for the quantitative estimation of albumin in the urine?

FIG. 11.

Esbach's Albuminometer.

By the use of Esbach's albuminometer (Fig. 11). This consists of a test tube of strong glass, marked near its middle and upper end respectively U and R, and near the bottom with small graduations marked respectively 1, 2, 3, 4, 5, 6, 7. It is used by filling up the tube with urine to the letter U and adding an acidulated picric acid solution to R. After 24 hours the coagulated albumin which has settled is read off in grammes of dry albumin per litre according to the small graduations to which it has settled. To obtain the percentage of dry albumin the respective figure is divided by 10. When the albumin is so abundant that the sediment is above 4, a more accurate result is obtained by first diluting the urine with one or two volumes of water and then multiplying the resulting figures by 2 or 3, as the case may be.

How is the acidulated solution of picric acid for this process prepared?

Dissolve 10 grammes picric acid and 20 grammes citric acid in 800 or 900 cubic centimeters of boiling water, which, on cooling, bring up with water to one litre (1000 c.c.).

Describe the volumetric estimation of albumin in the urine.

This consists of adding to 10 c.c. of urine 2 c.c. acetic acid, diluting with a little water, and then allowing Tanret's solution to drop in, drop by drop, from a suitable pipette, counting the number of drops so used; when the precipitate thus formed grows less, a drop of the urine is taken out and brought in contact with a few drops of 1 per cent. corrosive sublimate solution on a porcelain plate; if on mixing the two a red precipitate occurs, the reaction is complete, and for each drop so used, less 3 drops allowed for excess, 0.5 gramme of dry albumin per litre are present.

Give the composition of Tanret's reagent?

3.32 grammes potassium iodide, 1.35 grammes mercuric chloride, dissolved in 100 c.c. distilled water.

Is the presence of albumin in the urine alone sufficient for the diagnosis of Bright's disease?

No: as various other causes, already enumerated, may cause temporary or pseudo-albuminuria. If the amount of albumin, however, is large and persistently present, if the urine also contains casts and renal epithelium, the evidence points to the existence of renal disease.

Epithelial Cells in Urinary Sediments.

Are epithelial cells normally present in the urine, and, if present in larger quantities, what do they indicate?

Epithelial cells are always present in the urine, but according to their form, and the greater quantity present, they indicate pathological conditions of certain parts of the urinary tract.

What form have the epithelial cells of the uriniferous tubules?

They have a spherical, granular form, with faint outlines, but clearly defined nuclei. They may be present either singly or agglutinated as epithelial casts. The loops of Henle are lined with tessellated epithelium, and the straight tubules with the columnar variety (Fig. 12).

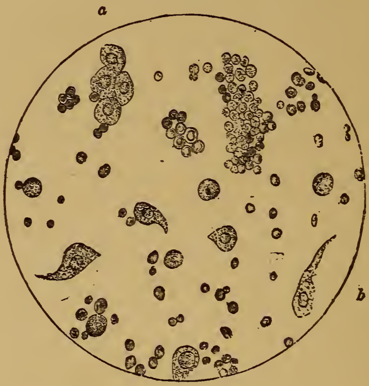
Which epithelial cells are derived from the renal pelvis?

Tessellated epithelium consisting of biconvex and caudate cells. The biconvex are generally as long again as they are broad. The caudate cells have an ovoid or club-shaped body ending in a fine point; their nuclei are well defined (Fig. 12).

Which epithelial cells belong to ureters and bladder?

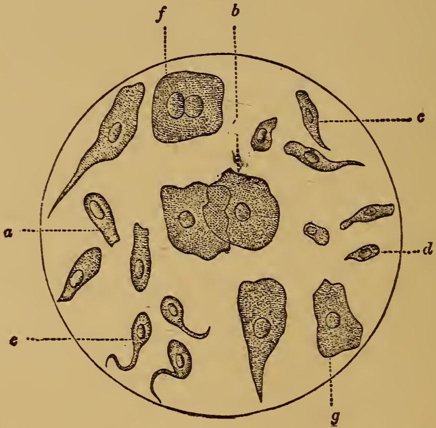
The ureters have regular tessellated epithelium, composed of polygonal cells, with central and clearly defined nuclei. The bladder has epithelium arranged in layers, of which the upper layer is formed by flattened polygonal cells; the deeper layers have a more spherical appearance (Fig. 13). While the female urethra has the same epithelium, that of the male urethra resembles more the renal epithelium. Renal epithelium is subject to pathological changes, such as fatty or amyloid degenerations, recognized by the microscope and the amyloid reactions.

FIG. 12.



Renal epithelial cells and epithelial cells from renal pelvis.

FIG. 13.



Epithelial cells. *a*, from male urethra; *b*, from vagina; *d*, from Cowper's glands; *e*, from Littré's glands; *f*, from female urethra; *g*, from bladder.

Tube Casts in the Urine.

Under what conditions are tube casts found in the urine, and how recognized?

In acute and chronic renal affections, tube casts may be recognized in the urinary sediment by means of the microscope. The sediment should be allowed to settle, and a specimen removed with a pipette for microscopic inspection. To make them more distinct a drop of Lugol's solution or aniline red may be added.

Which are the principal forms of tube casts?

The epithelial casts, composed of coherent epithelial cells of the tubes of Bellini; they are generally pale and transparent, and around them small round cells and nuclei may be recognized (Fig. 14).

Fig. 14.

Hyaline casts, also one epithelial cast.

The hyaline casts appear as pale, transparent cylinders of various sizes and configurations, and of very delicate outlines; they are also termed mucous casts (Fig. 14).

A modification of these with distinct outlines, slightly yellow color and waxy lustre are termed waxy casts (Fig. 15).

Granular casts (fibrinous casts), resemble the hyaline casts but have granular contents consisting of cells which have suffered granular change, giving them a darker appearance than the former. They may contain, also, oxalates, blood and pus corpuscles, fat globules and epithelial cells (Fig. 16).

FIG. 15.

Waxy casts.

FIG. 16.

Granular casts with fatty globules; also, blood and pus corpuscles, and epithelial cells.

Have the different tube casts always positive value for differentiating the various renal affections?

Not always, as in acute and chronic nephritis, as well as in amyloid degeneration, all the varieties may be present at one time.

When will they be of such diagnostic value?

When one variety only appears. Thus, if epithelial casts alone persist for several days, they point to the existence of a desquamative nephritis with favorable prognosis, while the simultaneous presence of pus corpuscles renders the prognosis less favorable.

In which cases of nephritis are hyaline and granular casts found?

In the severer cases with a disposition to chronicity, as indicated by their number and persistence. If they contain numerous fat granules and fat globules the diagnosis of fatty degeneration is justifiable, especially if accompanied by fatty degenerated renal epithelium both in the casts and separately.

What would indicate the existence of the contracted kidney?

If the tube casts grow thinner and the epithelial elements appear contracted.

How may amyloid degeneration be indicated?

The tube casts may here appear the same as in the other forms of nephritis, but there will be found besides the fatty degenerated epithelial cells, also such as have undergone amyloid degeneration, recognized by being colored red by methyl-violet, the others turning blue.

What would blood casts show?

That there is renal hemorrhage, the casts being coagulated blood with imbedded corpuscles.

Which are some of the other abnormal sediments of the urine of clinical interest?

Cystin, leucin and tyrosin, calcium oxalate and micro-organisms.

When and in what form is cystin found in the urine?

Cystin is found occasionally, but very seldom, as urinary concretion, also in urinary deposits; it is insoluble in water, not dissolved by heating, but soluble in alkaline hydrates, also mineral and oxalic acids. Under the microscope it appears in the form of colorless, shining, six-sided plates or prisms (Fig. 17).

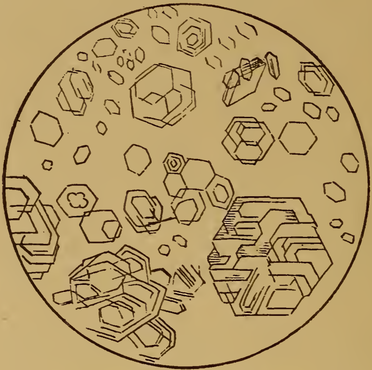
When and how do leucin and tyrosin occur in urinary sediments?

They occur frequently in the urinary sediments in acute yellow atrophy of the liver, also in phosphorus poisoning, and point to an incomplete oxidation of the albuminoids.

What is the microscopical appearance of leucin?

Yellow-colored spheres, at times concentrically striated with protruding delicate points or spines (Fig. 18).

FIG. 17.



Crystals of cystin (*after Ultzmann*).

FIG. 18.

(*a*) Leucin, spheres; (*b*) Tyrosin, needles and sheaves.

How does tyrosin appear under the microscope?

Tyrosin, which appears generally associated with leucin in urinary sediments, has the form of silky, white, microscopic needles which are arranged in sheaves or stellate form (Fig. 18).

In what compound is oxalic acid occasionally present in the urine?

As calcium oxalate, which is frequently found in the urine, but becomes of importance only when present in larger quantities and persistently, when it gives rise to oxaluria, signifying a retarded metabolism or suboxidation.

Describe the form of crystals of calcium oxalate in urinary sediments.

It forms minute, transparent, brilliant octahedra presenting somewhat the shape of a square envelope. At times the crystals assume the form of dumb-bells; to detect them a high power objective should be employed (Fig. 19).

FIG. 19.

Calcium oxalate in octahedral (envelope) crystals; also in dumb-bells; some larger crystals of uric acid.

Under which conditions are micro-organisms found in the urine?

As a rule, micro-organisms are found in the urine only after it has been exposed to the air for some time, but they may be carried into the bladder by catheters or sounds, and there set up ammoniacal decomposition of the urea, giving rise to cystitis. Of greater importance are those which are derived from the blood, as in infectious diseases, such as scarlatina, typhoid and malarial fevers and renal diseases.

Which are the principal micro-organisms found in the urine?

Mould (penicillium), yeast cells, sarcinæ (in the urine they are smaller than of the stomach), vibriones, bacteria, bacilli, cocci, etc. (Fig. 20).

FIG. 20.

Micro-organisms of urinary sediment.

Glycosuria.

Is sugar normally found in urine, and in what quantities?

Sugar as glucose is found normally in the urine in very small quantities, not more than 0.1 gramme in 24 hours.

If found in larger quantities and persistently, what pathological condition is present?

Glycosuria or diabetes mellitus; it may, however, be found in the urine in larger quantities in cerebral and nervous affections; also temporarily after anæsthesia from chloroform, ether, etc., as well as after copious ingestion of sugar.

What is the appearance and physical condition of the urine of glycosuria?

It is much increased in quantity, and may reach one or two gallons in the 24 hours; it is of pale or pale yellow color, often slightly greenish, clear, as a rule, but may contain sediments of urates or oxalates; it has a high specific gravity, generally between 1030 to 1040 and even more; the urea eliminated is abnormally increased.

Which foods increase and which diminish the amount of glucose in the urine?

Starchy and saccharine food increases, and animal diet decreases the amount.

In testing urine containing albumin for glucose, what has to be done first?

The albumin has first to be separated by boiling and filtration.

Describe Moore's test for the detection of glucose in urine.

In a long test tube mix about one part of urine with half its volume of liquor potassæ. Heat the mixed liquids in its upper half until active ebullition ensues, when, if glucose is present, the upper part will turn dark yellow to reddish brown. If the whole volume is thus treated, it will change color in a similar manner, and if then some nitric acid is added, it is decolorized and an odor of burnt sugar is given off.

What effect has glucose on certain metallic oxides if heated together in a strong alkaline fluid?

The metallic oxides, especially those of bismuth and copper, are reduced; the former to metallic bismuth, the cupric oxide to cuprous oxide.

Describe Bœttger's test.

Bœttger's, or the alkaline bismuth test, is performed by mixing equal parts of urine and liquor potassæ and adding a small quantity of bismuth subnitrate; boil for a minute or two, and if glucose is present, the bismuth will turn gray, brown or black, owing to the reduction to its metallic state.

What are the advantages and disadvantages of this test?

It has the advantage that uric acid, urates and kreatinin do not affect it, but albumin or sulphides present in the urine, produce similar effects as glucose.

What is Nylander's modification of the alkaline bismuth test?

This consists in the use of a single alkaline bismuth solution composed of bismuth subnitrate 2 grammes, Rochelle salt 4 grammes, solution of sodium hydrate (8 per cent.) 100 grammes. To 10 c.c. urine 1 c.c. of this solution is added and the two boiled together; if glucose is present, it turns brown or black.

Upon what reactions do the alkaline cupric tests depend?

First, that on adding a few drops of cupric sulphate solution to liquor potassæ a greenish-blue precipitate of cupric hydrate is formed.

$$CuSO_4 + 2KHO = Cu(OH)_2 + K_2SO_4.$$

Second, the cupric hydrate on boiling splits up into cupric oxide and water, the former appearing as a black precipitate.

$$Cu(OH)_2 = CuO + H_2O.$$

Third, the black precipitate does not form in the presence of certain organic matter and excess of alkaline hydrate, but remains in solution, having a deep blue color. When this alkaline cupric oxide solution is boiled in the presence of glucose, the latter takes away oxygen from the cupric oxide, leaving yellow insoluble cuprous oxide.

$$2CuO - O = Cu_2O.$$

Trommer's test, what is it, and how performed?

To some urine in a test tube add one-half or one-third volume of liquor potassæ and a few drops of a 10 per cent. solution of cupric sulphate. If this is heated in its upper half to the boiling point there will be a reddish-yellow turbidity, caused by the separation of cuprous oxide, if glucose is present. The two strata will give a distinct difference in appearance.

How can this test be improved by the addition of glycerin?

The addition of a few drops of glycerin will prevent the precipitation of the black cupric oxide and admit of the test solution being first tested by boiling. If to some liquor potassæ in a test tube a few drops of cupric sulphate solution are added, and also a few drops of glycerin, a clear, deep blue liquid will result. This is brought to the boiling point, and after removal from the flame a little of the urine is added; if glucose is present, the characteristic reddish-yellow cuprous oxide will form within a minute or two. If this does not take place after the first addition of the urine it should be brought to the boiling point again and a little more urine added as before.

Which is the principal alkaline cupric test, and how applied?

The Fehling's test, an alkaline solution of cupric oxide, which is held in solution by Rochelle salt (sodium-potassium tartrate), (see formula under quantitative tests for sugar). This solution is diluted with 3 to 4 volumes of water, heated to the boiling point, when a little urine is added. If sugar is present, a yellowish-red precipitate of cuprous oxide will form; if indistinct at first, boil again and add more urine. The boiling before adding the urine is necessary to establish the quality of the solution and to show if it does not decompose spontaneously at the boiling point.

What is the most positive evidence of glucose in urine, and how shown?

The alcoholic fermentation on addition of yeast. This may be shown by adding some yeast to a bottle filled with the suspected urine. Invert the bottle in a vessel containing the same urine; if inside of 24 hours part of the urine is displaced by carbon dioxide, glucose was present. This may be further verified by testing the urine for alcohol by adding to the fermented urine a few drops of potassium dichromate solution and sulphuric acid; if, on warming, a green color appears, alcohol was formed and glucose positively present in the urine.

How may the presence of glucose in urine be shown by phenyl-hydrazine?

To equal parts of urine and liquor potassæ add a few drops of phenyl-hydrazine, and heat to boiling. In the presence of glucose an intense yellow or orange color develops; on addition of an excess of acetic acid, yellow crystals are precipitated.

Which are some other very delicate tests for glucose in urine?

The tests with menthol, thymol or alpha-naphthol. These are applied by using their alcoholic solutions (1 to 7 alcohol), and mixing a few drops thereof with the urine. To the mixture, in a test tube, add some sulphuric acid in a manner that they do not mix, when, if glucose is present, there will be a red color at the line of contact with thymol or menthol, or violet with greenish borders if alpha-naphthol was employed.

How may picric acid be used for the detection of glucose in urine?

By its conversion, on boiling with an alkaline hydrate, into dark, reddish-brown picramic acid if glucose is present. Normal urine produces a similar reaction, but not of the deep reddish-brown color as when glucose is present.

By what ready method may the fermentation test for glucose in urine be used quantitatively?

By the differential density method of Roberts. This is conducted by accurately taking the specific gravity of the urine to be examined, the temperature of the urine being noted. With 4 ozs. of this urine in a 12 oz. flask or bottle, mix a small piece (about ¼ cake) of compressed yeast; after setting aside for 24 hours in a warm place, fermentation is completed. The urine is then cooled to the temperature of the former specimen and its specific gravity also accurately ascertained. The number of degrees of specific gravity lost by fermentation corresponds to the number of grains of glucose in the ounce of urine. The percentage may be obtained by multiplying the number of degrees lost by 0.22.

How is the quantity of glucose in urine ascertained by polarization?

By filling the container of a polarization apparatus with the filtered urine, free from albumin. The urine must be almost colorless, and care must be had that no air bubbles are in the tube. The analyzer is then moved to accurately correct the difference in color in the two halves of the visual field, and the angle through which it was moved is read off by means of the scale and vernier. The amount of glucose is computed by the following formula: $p = \frac{a}{+56\,l}$, in which p stands for the quantity of glucose in grammes in 1 c.c. of the urine, a the angle read off, + 56 the specific rotation for glucose, and l the length of the containing tube expressed in decimeters. Thus, if the angle read off were 4.5°, the tube 1 decimeter long, it would be $\frac{4.5^\circ}{56 \times 1} = 0.080$ glucose in 1 c.c., or 8.0 in 100 c.c. Various instruments for this purpose are in the market, some admitting the reading off directly of the percentage of glucose.

Give the formula for making Fehling's solution.

As Fehling's solution does not keep, it should not be kept on hand for any length of time, but should be made as two separate solutions, of which equal amounts by measure are mixed together at the time when wanted to form the complete test solution.

No. 1.	℞.	Cupric sulphate (pure, not effloresced, and free from water of crystallization),		34.64 grammes
		Water,	q. s. to	500 c.c.
No. 2.	℞.	Rochelle salt (crystallized),		173 grammes
		Solution of sodium hydrate, sp. gr. 1.34,		100 c.c.
		Water,	q. s.	500 c.c.

For use, mix equal volumes of No. 1 and No. 2 as needed.

Describe the method for the quantitative determination of glucose in urine by Fehling's volumetric process.

Place into a capsule, beaker or flask 10 c.c. of Fehling's solution diluted with 40 c.c. of water. Heat to the boiling point, and let gradually run into it from a burette a mixture of one part of urine and nine of water, stirring the mixture, and continue thus until the blue color of the test solution has entirely disappeared. The diluted urine is to be added in small quantities only, and the test solution must be raised to the boiling point after each addition, when it is left to subside for a few seconds to be able to view the supernatant fluid with transmitted light. Toward the last only a drop or two at the time should be added, as the clear shade should have a rather yellowish tint. This process should be repeated several times until the amount of diluted urine proves the smallest quantity effecting complete reduction.

How is the quantity of glucose computed from this?

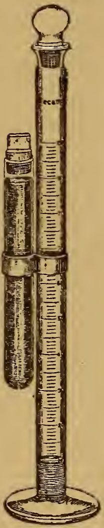
As 10 c.c. Fehling's solution are reduced by 0.05 gramme glucose, that amount of urine which is present in the dilution which has reduced the 10 c.c. of the Fehling's solution contained 0.05 gramme glucose. Thus, if 16 c.c. diluted urine (1 in 10) were used, 1.6 urine contained 0.05 gramme glucose. To obtain the percentage the following proportion will answer: 1.6 : 0.05 = 100 : x; x = 3. 1 per cent.

What is Johnson's picric-acid test for the quantitative determination of glucose in urine?

It consists of converting picric acid in the presence of potassium hydrate and glucose into reddish-brown picramic acid; the intensity of the color of the latter being proportionate to the amount of glucose present; the color of the picramic acid formed is then compared with that of a standardized solution of ferric acetate, and the amount of glucose ascertained by the dilution required.

How is this test performed?

FIG. 21.



Take of urine fʒj, liquor potassæ fʒss, solution of picric acid (gr. 5.3 to f℥j) ♏xl, water q. s. ad fʒiv into a test tube and boil for sixty seconds; cool the mixture and bring it up to the original volume (fʒiv). Of this pour 10 c.c. into a 100 c.c. graduated cylinder, which has attached to it a test tube of equal diameter and containing the standard fluid (Fig. 21); dilute the boiled mixture with distilled water to equal in color the standard liquid, and for each 10 c.c. it has been distilled up to, count 1 grain of glucose in the fluidounce of urine tested.

How may the measurement of the ingredients be simplified?

By taking 5 c.c. of each, urine, potassium hydrate solution (sp. gr. 1.036), solution of picric acid (gr. 3.5 to f℥j), and water.

Give the formula for the standard ferric acetate solution.

℞.	Liquor. ferri chloridi, U. S. P.,		fʒj
	Ammonii carb.,		ʒj
	Acidi acetici,		fʒv
	Aquæ destillatæ,	q. s. ad	f℥ iijss. M.

Is the above formula for the standard fluid reliable, and what should be done to make it so?

It is not reliable, and to make it so it should be standardized by comparing it with urine, to each fluidounce of which 1 grain of crystallized glucose has been added. To this the KOH, picric acid and water, is added, as above, and boiled for sixty seconds, when, after boiling, the standard iron solution is either diluted or made denser in color by addition of some liquor ferri chloridi to closely correspond in color. By doing so, not only is the error of variable strength of the ferric chloride solution corrected, but the error created by the normal presence of kreatinin is also overcome. When thus executed, this method is as reliable as any other for clinical purposes.

Lead and Mercury in the Urine.

Is lead readily detected in urine after lead-poisoning, and is a failure to find it proof of its absence from the system?

Lead is not always found in the urine after lead-poisoning, and is not always readily detected. Before testing for lead in the urine, iodide of potassium should be administered in full doses for a few days.

Give a method for detecting the presence of lead in the urine.

About 30 to 50 ounces of urine are brought to the boiling point in a porcelain evaporating dish, and while boiling, nitric acid (free from lead) is added in small quantities until on addition no further effervescence results; evaporation is then continued to dryness, the residue is carbonized in a porcelain crucible with the addition of nitric acid. The residuary mass, after combustion, is boiled out with nitric acid; after boiling it is diluted with water, the mixture filtered and the filtrate evaporated to dryness. The dry residue is dissolved in water slightly acidulated with HNO_3, and a current of hydrogen sulphide is allowed to pass through it for some time. If a brownish-black precipitate results, the presence of lead should be confirmed by testing another portion of the clear fluid with potassium iodide or neutral potassium chromate; with either of these it must give a yellow precipitate if lead is present. As the latter are not so sensitive as H_2S, it may be necessary to separate the precipitated lead sulphide, redissolve by gradual addition of HNO_3, evaporate excess of latter, and test after dilution and filtration as before. The lead iodide so derived will be seen under the microscope as six-sided plates. If the lead sulphide precipitated is sufficient, it may be reduced by the blow-pipe flame to a malleable particle of lead.

When may the detection of mercury in the urine be of diagnostic value?

In cases of protracted mercurialization, as in syphilis, etc.

Describe a ready method for detecting mercury in urine.

300–500 c.c. of urine are acidulated with hydrochloric acid and evaporated to about one-fourth of its volume, allowed to cool and then filtered. In the filtrate boil for a little while a slip of pure, bright copper foil; after boiling sufficiently, take it out, wash off in distilled water and dry it between bibulous paper; then roll up and put into an open glass tube; heat at the place where the copper is to redness, when the mercury will be driven to a cooler portion of the tube, to be recognized by the shape and brilliancy of its globules under the microscope; also, by converting it into red mercuric iodide, when into the hot portion of the tube a minimal fragment of iodine is introduced and its vapors are allowed to flow over the sublimed mercury.

What other very delicate method may be employed for detecting mercury in the urine?

The method of Ludwig is the one best adapted for detecting mercury in the urine. It is conducted by acidulating 200–500 c.c. urine with hydrochloric acid, warming the mixture to 50°–60° C., and adding 5 grammes of pure zinc dust (to be had of dealers in chemicals). The mixture is stirred for some time while warm, and then the zinc is allowed to subside, when the supernatant fluid is separated by decantation; the metallic sediment is well washed with distilled water and dried in a vapor bath after filtration. The mercury, having united with the zinc dust to form an amalgam, can now be driven off; this is done best in an open tube in which the zinc dust is secured by two loose asbestos plugs. The part of the tube containing the zinc is now heated and the mercury driven up to the upper and cooler portion of the tube. That portion of the tube is broken off, and the sublimed mercury is recognized by converting it into red mercuric iodide by passing a vapor of iodine over it.

DIETRICH'S TABLE (*Weight of one C. C. Nitrogen in Milligrams*).

Temp. C.	BAROMETRIC PRESSURE, IN MILLIMETERS.												
	720	722	724	726	728	730	732	734	736	738	740	742	744
10°	1.1338	1.1370	1.1402	1.1434	1.1466	1.1498	1.1529	1.1561	1.1593	1.1625	1.1657	1.1689	1.1721
11°	1.1288	1.1320	1.1352	1.1384	1.1415	1.1447	1.1479	1.1511	1.1542	1.1574	1.1606	1.1638	1.1670
12°	1.1237	1.1269	1.1301	1.1333	1.1364	1.1396	1.1428	1.1459	1.1491	1.1523	1.1554	1.1586	1.1618
13°	1.1187	1.1219	1.1251	1.1282	1.1314	1.1345	1.1377	1.1409	1.1440	1.1472	1.1503	1.1535	1.1566
14°	1.1136	1.1168	1.1200	1.1231	1.1263	1.1294	1.1326	1.1357	1.1389	1.1420	1.1452	1.1483	1.1515
15°	1.1085	1.1117	1.1149	1.1180	1.1211	1.1243	1.1274	1.1305	1.1337	1.1368	1.1399	1.1431	1.1462
16°	1.1034	1.1066	1.1097	1.1128	1.1160	1.1191	1.1122	1.1253	1.1285	1.1316	1.1347	1.1378	1.1409
17°	1.0983	1.1014	1.1045	1.1076	1.1107	1.1138	1.1170	1.1201	1.1232	1.1263	1.1294	1.1325	1.1356
18°	1.0930	1.0961	1.0992	1.1023	1.1054	1.1085	1.1117	1.1148	1.1179	1.1209	1.1241	1.1272	1.1303
19°	1.0877	1.0908	1.0939	1.0970	1.1001	1.1032	1.1063	1.1094	1.1125	1.1156	1.1187	1.1218	1.1248
20°	1.0825	1.0855	1.0886	1.0917	1.0948	1.0979	1.1009	1.1040	1.1071	1.1102	1.1133	1.1164	1.1194
21°	1.0771	1.0802	1.0832	1.0863	1.0894	1.0924	1.0955	1.0986	1.1017	1.1047	1.1078	1.1109	1.1139
22°	1.0717	1.0747	1.0778	1.0808	1.0839	1.0870	1.0900	1.0931	1.0961	1.0992	1.1023	1.1053	1.1084
23°	1.0662	1.0692	1.0723	1.0753	1.0784	1.0814	1.0845	1.0875	1.0906	1.0936	1.0967	1.0997	1.1028
24°	1.0606	1.0636	1.0667	1.0697	1.0728	1.0758	1.0789	1.0819	1.0849	1.0880	1.0910	1.0940	1.0971
25°	1.0550	1.0580	1.0610	1.0641	1.0671	1.0701	1.0732	1.0762	1.0792	1.0823	1.0853	1.0883	1.0913

	746	748	750	752	754	756	758	760	762	764	766	768	770
10°	1.1753	1.1785	1.1817	1.1848	1.1880	1.1912	1.1944	1.1976	1.2008	1.2040	1.2072	1.2104	1.2136
11°	1.1701	1.1733	1.1765	1.1717	1.1829	1.1860	1.1892	1.1924	1.1956	1.1988	1.2019	1.2051	1.2083
12°	1.1649	1.1681	1.1713	1.1744	1.1776	1.1808	1.1839	1.1871	1.1903	1.1934	1.1966	1.1998	1.2029
13°	1.1598	1.1630	1.1661	1.1693	1.1724	1.1756	1.1787	1.1819	1.1851	1.1882	1.1914	1.1945	1.1977
14°	1.1546	1.1577	1.1609	1.1640	1.1672	1.1703	1.1735	1.1766	1.1798	1.1829	1.1861	1.1892	1.1923
15°	1.1493	1.1525	1.1556	1.1587	1.1619	1.1650	1.1681	1.1713	1.1744	1.1775	1.1807	1.1838	1.1869
16°	1.1441	1.1472	1.1503	1.1534	1.1566	1.1597	1.1628	1.1659	1.1691	1.1722	1.1753	1.1784	1.1816
17°	1.1397	1.1419	1.1450	1.1481	1.1512	1.1543	1.1574	1.1605	1.1636	1.1667	1.1699	1.1730	1.1761
18°	1.1334	1.1365	1.1396	1.1427	1.1458	1.1489	1.1520	1.1551	1.1582	1.1613	1.1644	1.1675	1.1706
19°	1.1279	1.1310	1.1341	1.1372	1.1403	1.1434	1.1465	1.1496	1.1527	1.1558	1.1589	1.1620	1.1650
20°	1.1225	1.1256	1.1287	1.1318	1.1348	1.1379	1.1410	1.1441	1.1472	1.1502	1.1533	1.1564	1.1595
21°	1.1170	1.1201	1.1231	1.1262	1.1293	1.1324	1.1354	1.1385	1.1416	1.1446	1.1477	1.1508	1.1539
22°	1.1115	1.1145	1.1176	1.1206	1.1237	1.1268	1.1298	1.1329	1.1359	1.1390	1.1421	1.1451	1.1482
23°	1.1058	1.1089	1.1119	1.1150	1.1180	1.1211	1.1241	1.1272	1.1302	1.1333	1.1363	1.1394	1.1424
24°	1.1001	1.1032	1.1062	1.1092	1.1123	1.1153	1.1184	1.1214	1.1244	1.1275	1.1305	1.1336	1.1366
25°	1.0944	1.0974	1.1004	1.1035	1.1065	1.1095	1.1126	1.1156	1.1186	1.1216	1.1247	1.1277	1.1307

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