ably all owe their value almost entirely to their antiseptic action. The remedies promising most are urotropin, buchu, uva ursi, pareira brava, and chimaphila. Urotropin is best given in doses of five grains three times a day. The dose of the fluid extract of each of the other drugs mentioned is a teaspoonful, well diluted, three or four times a day. These all have a slight antiseptic action, as shown by the diminished tendency to decomposition when the urine is left standing. This is particularly true of urotropin, but in very large doses it may cause some frequency of urination by rendering the urine too acid. Uva ursi has some diuretic action, as has also chimaphila. Buchu does not increase the amount of urine appreciably. In the very chronic form the stigmata of Zea Mays will be found a more effective remedy, as they stimulate the renal epithelium directly. A teaspoonful of the fluid extract may be given every four hours. In rare cases, in which something stimulating is required, small doses of turpentine may be of value. If the pyelitis be associated with renal calculus, a surgical operation, with removal of the stones and temporary drainage of the kidney, offers the best hope of permanent relief. By correcting the reaction of the urine we may prevent any increase in the size of the stones, but the chance of causing them to dissolve is remote. Hyoscyamus, phenacetin, belladonna, and opium in its various preparations, afford temporary relief. Sweet spirits of nitre at times helps and may relieve the vesical tenesmus, which is often associated with this disease. In tuberculous cases there is little hope of permanent relief except through nephrectomy or through the breaking down and complete disappearance of the organ, in consequence of which it will cease altogether to secrete any urine. In these cases the pain is often referred to parts of the urinary tract which are situated lower down and which are not involved in the disease.

In the cases due to diminution of the size of the bladder from extraneous causes the removal of those causes at once suggests itself. In prostatic hypertrophy the flow from an overdistended bladder may easily be mistaken for abnormal frequency of urination. This possibility should be investigated before seeking for a further cause. Overdistention may also occur in connection with a stricture of small calibre. Drawing off the residual urine under the strictest aseptic precautions one or more times daily may entirely relieve the symptoms. The administration of five grains of urotropin three times a day diminishes the danger of cystitis. In cystitis an antiseptic which will be eliminated in the urine is indicated. In many cases washing out the bladder once or twice a day with an antiseptic solution, such as a four-per-cent. solution of boric acid, is necessary. When stronger antiseptic washes are needed, one of permanganate of potassium or of citrate of silver will be found serviceable. Nitrate of silver is more stimulating and should seldom be used in solutions of more than one grain to the ounce. Pareira brava is said to be useful in chronic catarrh of the bladder. It checks bleeding in these cases and diminishes the muco-purulent secretion. Cubebs, copaiba, and sandal-wood, though more effective in irritation of the urethra, exert their influence through the medium of the urine and are of use in bladder affections. This is especially so of the oil of sandal-wood. All of these drugs resemble each other closely. It should be borne in mind that while they are being taken the urine is somewhat irritating. When they are given in large doses, they give rise to a constant desire to urinate, and the pain and difficulty in doing so are great. In some cases, in which the bladder and urethra are much inflamed, the pain may be so great as to lead to complete retention. The ordinary dose of each of these drugs is ten minims three times a day. They are best given in capsules, as the taste is disagreeable. Even in doses of ten minims twice a day the oil of sandal-wood at times gives so much backache that it has to be discontinued.

For the relief of the pain and frequency of urination associated with the presence of a calculus in the bladder, operation alone is of any avail. Morphine or belladonna or a combination of the two may afford great temporary relief.

At times we are forced to abandon our search for a tangible cause and fall back upon a neurosis as an explanation of the trouble. Here we may expect relief from the use of nervous sedatives, such as one of the bromides or hyoscyamus. Treatment of the condition through the urine proves as a rule unsuccessful, and washing out the bladder often only aggravates the patient's suffering. In the tenesmus of tuberculosis washing the bladder is generally worse than useless, especially if we have to pass a catheter for this purpose.

In the cases in which we need urinary sedatives, when the cause lies in the urethra itself, copaiba, sandal-wood oil, and cubebs give great relief. In the intense burning which accompanies micturition and which does not yield to internal medication or local treatment, the injection into the urethra of a two-per-cent. solution of cocaine alleviates the distress temporarily. In men, urination with the penis submerged in water as hot as can be borne, often gives relief.

Finally, in those cases of incontinence in children in which the trouble does not yield to belladonna in full doses, and appears to be caused by an irritable bladder, circumcision at times effects a cure.

Franklin G. Balch.

URINE.—Physical Properties. Quantity.—The amount of urine voided is dependent (1) on the state of the renal epithelium; (2) on the rapidity of the blood flow through the kidneys. It is independent of the blood pressure.

A normal healthy adult of the average weight of 75 kgm. passes from 1,500 to 2,000 c.c. of urine in twenty-four hours. Infants pass absolutely less, but, in proportion to their body weight, relatively more urine; this is largely due to the liquid diet. Abundant ingestion of fluids increases diuresis (*urina potus*); sweating (violent exercise, hot weather) decreases it. Less urine is normally passed at night than during the day; in chronic nephritis this ratio may be reversed.

Pathology.—Destructive renal lesions or local circulatory disturbances, in order to influence the flow of urine, must be bilateral; unilateral interference with diuresis is compensated by the healthy organ.

(*a*) *Polyuria.* The more chronic the nephritis the greater the tendency to polyuria (contracted kidney, amyloid). This is chiefly due to the contraction of the renal tissues and the resulting acceleration of the blood flow. During convalescence from acute nephritis; in heart and lung disease as soon as the circulatory disturbances begin to be compensated; in diabetes mellitus, and insipidus; after psychic shocks, and in various neuroses (*urina spastica*); after the exhibition of certain drugs (see *Diuretics*), and after the ingestion of certain articles of food (tea, coffee, alcohol, etc.)—the flow of urine is increased.

(*b*) *Oliguria.* In acute nephritis, in acute exacerbations of chronic nephritis, and in heart and lung diseases leading to stasis the flow of urine is decreased.

(*c*) *Anuria.* In uræmia (occasionally), in diseases causing great loss of fluids through other emunctories than the kidneys (acute gastritis and intestinal catarrh, with profuse vomiting and diarrhœa, cholera, dysentery), in rapidly progressive forms of anæmia, and in hysteria, the urine may be altogether suppressed.

Determination.—The urine should preferably be collected from morning to morning before eating; the bladder should be emptied before the collection is begun; the patients should urinate before going to stool, as, particularly in old women, much urine may be lost during the act of defecation. The total quantity may be measured or determined by weighing; the weight multiplied by the specific gravity yielding the volume. For clinical purposes the former method is best; for exact determinations the latter is to be preferred.

The Specific Gravity.—The specific gravity of the urine is, as a rule, high when little urine is voided and

low when the flow of urine is abundant. The same factors, therefore, that determine physiological fluctuations in the amount of urine also determine corresponding fluctuations in its specific gravity. As the normal total quantity varies from 1,500 to 2,000 c.c., so the normal specific gravity varies correspondingly from 1.025 to 1.015.

The specific gravity of the urine is an index of the excretion of urinary solids. If the latter were all heavier than water, the last two figures of the specific gravity (expressed in four figures) would directly indicate the quantity by weight of urinary solids contained in one litre of urine. As some of the excreta are, however, heavier than water, or of the same specific gravity, their weight is greater than indicated by these two figures. It has been found empirically that the last two figures of the specific gravity multiplied by 2.2337 give the weight in grains of the solids in one litre of the urine. [Example: Specific gravity = 1.018; 18 multiplied by 2.2337 = 40.2066 grains of solids in one litre of urine.] This calculation, while not absolutely accurate, is useful for comparative studies.

Pathology.—In severe *febrile diseases* the specific gravity is usually low without a corresponding increase of urine as soon as the patient's vitality begins to flag and general metabolism is reduced.

In *acute and subacute nephritis* the specific gravity is usually high, the water excretion correspondingly reduced. In the healing stage of acute nephritis the flow often increases, whereas the specific gravity remains low; this indicates that the kidneys are regaining their power to excrete water, but not as yet to eliminate solids. In acute exacerbations of *chronic nephritis* and in the terminal stages of destructive inflammation and degeneration of the kidneys the specific gravity is reduced; when it occurs suddenly, this is a bad prognostic omen, and often indicates threatening uræmia. In contracted kidney the specific gravity is low and the flow abundant. In diabetes mellitus the flow is great and the specific gravity very high, whereas in diabetes insipidus the flow is also great, but the specific gravity very low.

Determination.—The specific gravity may be determined (*a*) by weighing with a hydrostatic balance, (*b*) with a pyknometer, and (*c*) with an aerometer. The first method is useful only in very exact work, and requires a complicated balance; it will not be described here. The second and third methods are useful for clinical work. In ordinary comparative studies the aerometer is quite sufficient.

The *pyknometer* is a flask with a long neck that is drawn out in one place (see Fig. 4852); at the narrowest point is a mark; the flask is closed with a ground-glass stopper. The flask is first filled with distilled water to the mark and weighed; it is then filled with the filtered urine to the mark and weighed again. The weight of the urine divided by the weight of the water gives the specific gravity. It is very important that the temperature of the water and that of the urine should be exactly alike when the pyknometer is filled and when it is weighed. For other forms of pyknometers than the one shown in Fig. 4852, see text-books.

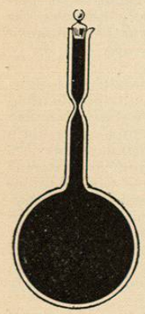

Fig. 4852.—Pyknometer.

The *aerometer* (urometer). This instrument consists of a glass cylinder and a float (see Fig. 4853). The latter should be graduated from 1.000 to 1.040. It is better to have two floats, the one reading from 1.000 to 1.020 and the other from 1.020 to 1.040. The urine is poured into the cylinder, the float introduced into the urine, and the specific gravity read off directly from the aerometer scale. Here, too, the temperature is important; it should be about 17.5° C., for the aerometers are graduated at this temperature. If the urine is warmer than 17.5° C., one-third of a urometer degree should be added for each degree of temperature; if the urine is colder than 17.5° C., the reading should be corrected by subtraction—one-third urometer degree for each degree of temperature. [Example: Urine 20.5° C., specific gravity 1.017. Corrected, $1.017 + 3 \times \frac{1}{3} = 1.018$.] A temperature scale is found on many urometers.

Reaction.—Normal urine is never neutral to litmus; it is either acid, amphoteric, or alkaline. The acidity is never due to the presence of free acid, but to the excess of acid salts (monobasic phosphates and urates) over alkaline salts (dibasic phosphates and urates). When the two are mixed in certain definite proportions the reaction becomes amphoteric. The urine becomes alkaline after eating (HCl—secretion) and after the ingestion of certain salts of vegetable origin (citrates, tartrates, etc.), as the latter are excreted as carbonates. Old urine is usually alkaline as the micrococcus ureæ generates ammonium carbonate.

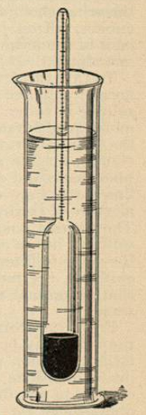

Fig. 4853.—Aerometer.

Pathologically the acidity of the urine is always increased in febrile processes, for here increased katabolism of proteid with liberation of sulphuric and phosphoric acids from proteid-sulphur and proteid-phosphorus occurs. In leukæmia, scurvy, and diabetes the urine is also in general acid.

Increased alkalinity is a valuable sign only if the above-named physiological factors can all be excluded. It is important to determine whether the urinary alkalinity is due to the liberation of ammonia or to the presence in solution of fixed alkali. Free ammonia signifies fermentation of the urine and points to cystitis. Fixed alkali appearing in excess in fresh urine may be due to the withdrawal of acid from the body (vomiting and frequent lavage), to the admixture of alkaline secretions from the urinary passages, or to the rapid absorption of exudates and transudates.

Determination.—For clinical purposes the litmus test is sufficient: blue litmus paper turning red in acid urine, and red litmus paper turning blue in alkaline urine. If the blue color remains after the paper dries, the alkalinity is due to fixed alkali; if it vanishes, to free ammonia.

Optical Properties.—(*a*) *Color.* The color of the urine is dependent on its concentration, its reaction, and the pigments it contains. Normal urine may be from pale yellow to reddish-brown. The greater the concentration the darker the color. Acid urine becomes more pale when it is alkalinized, and alkaline urine darker when it is acidified.

Certain pathologic pigments change the color of the urine. Bile pigment colors it green or brown, blood pigment red to brown red, urobilin dark brown, and melanin brown to black. Certain aromatic decomposition products that are found in the body (indican, phenols) cause the urine to turn dark on standing. Certain fruits (cherries, raspberries, etc.) and certain medicaments impart a characteristic color to the urine (see carbolic acid, coal-tar preparations, resorcin, naphthol, salol, chrysarobin, rheum, senna, santonin, etc.).

(*b*) *Fluorescence.* Pale yellow normal urine shows a bluish, yellowish-red urine, a greenish or yellow fluorescence. Urine containing albumin shows more fluorescence than normal urine, and ammoniacal urine more than urine that is not decomposed.

(*c*) *Behavior toward Polarized Light.* Normal urine is almost always slightly lævorotary; it is never dextrorotary, and hardly ever optically inactive. The presence of certain abnormal constituents (dextrose, levulose, glycuronic acid, etc.) produces typical polarimetric phenomena that will be described below.

(*d*) *The Spectrum.* Normal urine shows no absorption bands, but the coefficient of light extinction varies in different regions of the spectrum. In pathologic urines hæmatoporphyrin, uroerythrin, and urobilin produce typical spectra (see below).

Odor.—Fresh normal urine has a characteristic odor that is not disagreeable. The disagreeable, so-called, urinous odor is due to the presence of bacterial decomposition products (probably ammonia and phenols). Occasionally the urine emits an odor of H_2S (hydrothionuria). Certain substances impart a characteristic odor to the urine when taken by mouth (valerian, garlic, copaiba, cubebs, saffron, turpentine [violets], etc.). The peculiar odor of the urine after eating asparagus is due to methylmercaptan.

Transparency.—Normal acid urine is clear, for the normal acid and neutral salts of the urine are all readily soluble in water. Normal acid urine becomes cloudy if more quadriurate is excreted than can be dissolved in the urinary water. Normal alkaline urine is always cloudy, for the alkaline salts of the urine (*i.e.*, normal phosphates and carbonates and diphosphates of the alkaline earths) are essentially insoluble in water or in the mixture of neutral and acid salts in solution in the urine. The proteid constituents of clear urine are not in true solution, but in colloidal solution; hence the tendency of the urine to filter with decreasing rapidity. The scanty epithelia, the mucin bodies, and the crystals in suspension in normal urine form a fine cloud (nubecula) on standing.

Freezing Point (Cryoscopy).—The freezing point of the urine may be considered an index of the osmo-regulating function of the kidneys. The attempt has been made to utilize freezing-point determinations ("cryoscopy") in the diagnosis of renal diseases. The results obtained so far by different investigators are, however, ambiguous, even contradictory, so that this method is for the present of subordinate importance. This field is nevertheless promising, and as soon as the technique shall be simplified and perfected cryoscopy may become a valuable laboratory adjuvant to diagnosis. For a review of the complete literature to date see H. Strauss: *Zeitschr. f. klin. Med.*, 1902, vol. xlvii., pp. 337 to 407.

Electric Conductivity.—The resistance offered by the urine to the passage of an electric current has been utilized in order to determine the quantity of mineral salts present in the urine. There is without doubt a connection between the total ash of the urine and its conductivity. Only those urinary constituents can be estimated by determining the electrical conductivity that are electrolytes, and it might be imagined that the large number of non-electrolytes that may be present in normal and pathological urines would interfere with this determination. It has been shown, however, that such bodies as urea, uric acid, even sugar and albumin in the quantities ordinarily present in pathologic urine, exercise only a very small effect in lowering the conductivity of the urine. The conductivity of the urine is essentially, therefore, a function of the total mineral content, and the determination has a significance similar to that of the determination of the specific gravity. It is, however, more accurate. This method, when simplified as to technique, will prove a valuable aid in the determination of the eliminatory power of the kidneys for inorganic constituents. In combination with similar determinations with the blood serum it promises to throw much light on the pathology of renal insufficiency and of a variety of metabolic disorders.

CHEMICAL EXAMINATION.

Organic Constituents.

The Albumins.—*Albuminuria.—Physiological Albuminuria.* Every urine contains traces of albumin that are derived from cellular elements. This albumin is nucleo-albumin and differs from the albumins of the serum; the quantities normally present in the urine are so small that they cannot be detected by ordinary tests; the substance must first be isolated from large quantities. Every albuminuria of an *hæmatogenic* type must be considered pathological, and the conception of a *physiological* excretion of serum-albumin that some authors advocate should be discarded. All that the term physiological albuminuria implies is that a small quantity of blood albumin may occasionally be excreted in apparently healthy subjects; that this albuminuria may be transitory, and that it may lead to no serious consequences. A biologic phenomenon, however, because it is innocent, need not, therefore, be physiological. Transitory albuminuria in otherwise healthy persons (muscular exercise, cold bathing, pregnancy, and psychic shock) must always be attributed to circulatory disturbances in the kidneys or to slight nutritional impairment of the glomerular or tubular epithelia. Subjects with such albuminurias should always be considered predisposed to proper renal disease.

Pathological Albuminuria. Fluids containing albumin (pus, blood, lymph, cystic fluid, and sperma) may enter the urine below the kidneys (*albuminuria spuria extra-renalis; pseudo-albuminuria*), or soluble albumin may enter the urine within the kidneys from the blood (*albuminuria vera-renalis*). The two forms can usually be differentiated without difficulty. In *A. extra-renalis* the centrifuged and filtered urine contains only a small percentage of albumin as compared to the number of cellular elements in the sediment. If the latter consists of pure pus, the albumin percentage in the filtrate compared with the number of cellular elements in 1 mm.³ of the sediment should be as 1:50,000. If it exceeds this proportion, then the albuminuria should not be considered due to the admixture of pus alone. In affections of the kidneys that produce only a slight degree of true albuminuria (contracted kidney) the combination of extra-renal albuminuria (*e.g.*, cystitis) and renal albuminuria may be difficult to recognize. Here the study of the cellular sediment, on the one hand, of general clinical symptoms (heart, arteries, and retina), and of certain peculiarities of the urine (quantity and specific gravity) on the other, must determine the diagnosis.

In *A. renalis* the excretion of albumin may be due to (1) inflammatory and degenerative lesions of the renal tissues; (2) circulatory disturbances in the kidneys; (3) certain febrile diseases (bacterial toxins and lowered blood pressure); (4) anæmia and cachexia (hæmatogenous albuminuria). Finally, there are certain forms of cyclic and intermittent albuminuria of unknown etiology occurring in healthy subjects or in sufferers from very chronic types of nephritis.

In acute nephritis the percentage of albumin is high (as high as five per cent., although usually not above one per cent.). In certain chronic forms of nephritis the percentage may be equally high. As a rule, however, the more chronic the nephritis the smaller the percentage of albumin. In very chronic forms there may even be no albumin at all.

In true albuminuria the urine may contain the following albumins alone or in combination: (1) Serum-albumin (serin); (2) serum globulin (paraglobulin); (3) mucin (nucleo-albumin); (4) albumose; (5) peptone; (6) fibrin (fibrinogen?); (7) hæmoglobin (methæmoglobin); (8) "Bence-Jones albumin"; (9) histon and nucleo-histon.

Serum Albumin and Globulin.—These two albumins almost invariably occur together in pathological urine. The proportion of the two, the so-called "albumin quotient" (serum-globulin), varies greatly in different cases. It may, moreover, differ not only from the quotient of normal serum, but also of the serum of the nephritic patient. The tests for serum-albumin and globulin may be described together.

Tests. Only those four tests are given here that are of value clinically and that render it possible to differentiate these albumins from albumoses, nucleo-albumins, etc. For the numerous other albumin reactions I refer to text-books of physiological chemistry.

1. The Nitric Acid Test.—A small quantity of cold filtered urine is poured into a test tube and a few cubic centimetres of concentrated nitric acid allowed to slowly flow down the sides of the vessel. If albumin is present, an opaque zone forms at the plane of contact; if the amount of albumin is small, the ring may not form for one or two minutes.

Urates, certain balsams, and resins may form a similar ring; the albumin ring, however, begins at the plane of contact and extends upward, whereas the urate ring is more apt to begin above the plane of contact and gradually extend down to the acid. The urate ring, moreover, does not appear if the urine is well diluted. It also disappears on heating. The ring produced by balsams and resins is soluble in ether, and may be made to disappear by heating the liquid with this solvent. Nucleo-albumin and albumoses also form a ring with nitric acid. The test should always be repeated with diluted urine; if the ring becomes thicker in the diluted urine, the presence of nucleo-albumin is rendered probable. The albumose ring disappears on heating and reappears on cooling, the liquid meanwhile turning bright yellow; if the liquid becomes only partially clear on heating, albumin and albumoses may be present together. Urea, if present in large quantities, may crystallize out in this test as urea-nitrate and form a white zone above the acid. The crystalline character of this precipitate usually reveals its origin. If the urine contains much pigment or indoxyl multicolored rings may appear below the albumin ring.

2. The Boiling Test.—The urine is slightly acidulated with acetic acid and boiled. A flocculent precipitate may be due to the presence of albumin or of earthy phosphates. One or two drops of nitric acid for every cubic centimetre of the urine are now added; if the precipitate dissolves, it consisted of phosphates; if it does not dissolve, or if it becomes more intense, it consisted of albumin. Care must be taken to add just enough nitric acid, for, if too little is added, only a portion of the basic phosphates is converted into acid phosphates and the albumin in combination with a base (albuminate) remains in solution; if too much nitric acid is added, albumin-nitrate forms, and this, too, remains dissolved. The danger of dissolving the albumin in an excess of acid is decreased if acetic acid is used instead, and if the urine, prior to boiling, is mixed with one-sixth volume of saturated sodium chloride solution.

Bence-Jones albumin also coagulates on heating in acid urine, but at a low temperature (50° C.), and on boiling this coagulate disappears. Albumoses and nucleo-albumins (mucins) are not precipitated by this test.

3. The Potassium Ferrocyanide Test.—This is the most delicate one of the ordinary clinical tests. The urine is rendered strongly acid with acetic acid and a ten-per-cent. solution of potassium ferrocyanide, added drop by drop. If albumin is present even in traces, a cloudiness appears at once; if large quantities are present, a flocculent precipitate appears. In this test the urine should first be filtered until it is clear; if owing to the presence of microbes the urine cannot be cleared, a specimen of the urine should always be compared with the specimen treated with the reagent in order to determine whether the cloudiness has become more pronounced in the latter. It is well to dilute the urine for this test.

Albumoses are also thrown down, but they dissolve on boiling the liquid and reappear on cooling. If the urine contains much mucin or urate, precipitates form when the acetic acid is added; but they can both be made to disappear if the urine is warmed.

4. The Biuret Reaction.—The urine is treated with potassium hydrate solution and a ten-per-cent. copper sulphate solution added drop by drop. In the presence of albumin alone the liquid turns pure violet; in the presence of albumoses or peptones it turns rose; if albumin and albumoses or peptone are present together, the urine assumes tints intermediary between violet and rose. If small quantities of albumins are present, care must be exercised not to add too much copper solution, as otherwise the violet or rose tint is obscured by the blue of the reagent.

Special Test for Globulin.—The excretion of globulin is of subordinate clinical interest; only a few cases are on record in which it appeared alone in the urine; occasionally, however, it may be desirable to examine the urine for its presence. The following method is practical:

The urine is mixed with an equal volume of saturated ammonium- or magnesium-sulphate solution; this precipitates the globulins and albumoses, but leaves the serum-albumin in solution (the latter being precipitated only if the urine is saturated with the above salts). The precipitate is dissolved in one-per-cent. soda solution and the liquid acidified with acetic acid. Albumoses remain in solution while globulins are precipitated, and this precipitate, moreover, is insoluble in sodium chloride solution.

Quantitative Estimation of Coagulable Albumin.—For accurate determinations a measured quantity of the urine should be acidified and boiled, the coagulate collected in a weighed filter, washed with water, alcohol, ether, dried to a constant weight, and weighed. A nitrogen determination is then made with a portion of this residue (Kjeldahl method, see below), and the value obtained multiplied by 6.25 (albumin contains 16 per cent of N; if therefore we find X nitrogen, this corresponds to $\frac{100}{16} = 6.25$ times X of albumin). The figure obtained by this multiplication indicates in grams the amount of albumin present in the quantity of residue used for the determination. From this the amount present in the total urine can be calculated.

Fig. 4854.—Esbach's Albuminometer.

For ordinary clinical purposes of comparison the method of Esbach is sufficiently accurate. The method is based on the precipitation of albumin by picric acid. The apparatus used is called Esbach's albuminometer (Fig. 4854) The tube is filled with urine to *U* and with reagent to *R*. The two liquids are thoroughly mixed by inverting the tube several times. The apparatus is then allowed to stand for twenty-four hours at room temperature and the height of the column of precipitate determined. The figures ½ to 7 on the apparatus below *U* indicate the amount of albumin in grams per litre of urine; if, therefore, *e.g.*, the height of the column of coagulate corresponds to 3, the urine contains 3 gm. of albumin to the litre (1,000 c.c.), or 0.3 per cent. Esbach's reagent is 10 gm. of picric acid and 20 gm. of citric acid dissolved in 1 litre of water. In this test the reaction of the urine should be acid, its specific gravity not above 1.010, and it should not contain more than 0.4 per cent. of albumin; otherwise the determination is not accurate. It will be necessary, therefore, as a rule, to dilute and acidify the urine prior to making the determination. Occasionally the precipitate of albumin will not settle; then this method cannot be employed; nor can it be employed if the urine contains quinine or antipyrin.

Nucleo-Albumin (Mucins).—The mucin of the older writers has been shown to consist of albumin in combination with one of these acids that are usually present in the urine, viz., nucleinic acid, chondroitin-sulphuric acid, and taurocholic acid. On the addition of acetic acid to the urine these compounds are precipitated as nucleo-albumin, chondro-albumin, and albumin taurocholate. These bodies alone or combined form "mucin," and it is quite clear that the character of this substance must vary according to the relative quantities of these acids present in the urine. The taurocholate is often absent from normal urine, but it is present in abundance in icteric urine. Chondro-albumin is a glycoproteid and can be split into proteid and carbohydrate, while nucleo-albumin is a "phosphorous proteid" and can be split into proteid and nuclein.

Mucins are always present in traces in normal urine. They are excreted in excess in desquamative catarrh of

the urinary passages, in infectious forms of nephritis (diphtheria and scarlatina), in toxic nephritis (tar, pyrogallol, corrosive sublimate, arsenic), in typhoid fever, in croupous pneumonia (disappearing within twenty-four to forty-eight hours after the crisis), after chloroform anæsthesia, and, particularly, in icterus.

Tests. Clouding of the diluted urine with acetic acid speaks for the presence of mucin bodies; if the mixture is shaken with chloroform or ether, a cloudy ring of mucin forms at the plane of contact after the liquids have been allowed to separate. Mucins give the nitric acid test (see above), but the ring of coagulate first forms 0.5 to 1 cm. above the acid and later extends down to it. If the urine is sufficiently diluted, the urate ring, that behaves similarly, is not formed. In order fully to identify the substance it must be isolated from large quantities of the urine (see text-books of physiological chemistry).

Albumoses and Peptone.—It is doubtful whether peptone (in the sense of Kühne) ever appears in the urine. Recent investigations have shown the peptones of the older writers to be albumoses (hemialbumose, deuteroalbumose [peptone in the sense of Brücke], propeptone, histon, etc.). All these bodies appear in the urine when the intracellular disassimilation of the proteids is perverted as the result either of bacterial invasion (suppuration, tuberculosis), or of intoxication with certain inorganic poisons (phosphorus), or of certain metabolic disorders of unknown pathogenesis (osteomalacia). Pyogenic "peptonuria" is clinically important, for the diagnosis of "pus somewhere" may frequently be strengthened by the appearance of albumoses in the urine; the differentiation is also occasionally possible, with the aid of this sign, between purulent and tuberculous or simple serous exudates (meningitis, pleuritis, etc.).

Tests. In order to get rid of the common albumins the urine is treated with an equal volume of saturated salt solution, acidified with acetic acid and boiled. The solution is filtered hot; coagulated albumins remain behind while albumoses go into the filtrate from which they separate on cooling. The filtrate should give the biuret reaction (see above), and the precipitate formed on cooling should redissolve on boiling.

The differentiation of the different albumoses that may be present in the urine is possible, but the chemical manipulations incident to this separation are so complicated that a description of these methods lies beyond the scope of this article. (For an excellent exposé of the subject see Neubauer u. Vogel, "Harnanalyse," 1898, pp. 466 to 484.)

Fibrin (*Fibrinogen*).—These bodies occasionally appear in the urine in chyluria and in hæmaturia, also in croupous inflammation of the urinary passages (tuberculosis, diphtheria). Fibrinogen only appears in profuse hæmaturia, and its presence may be suspected from the formation of coagula in the urine; the latter may form either within the urinary passages or not until the urine is voided.

Test. The coagula are filtered off, repeatedly washed with a five- to ten-per-cent. solution of NaCl dissolved in a boiling one-per-cent. soda solution, or in a 0.5-per-cent HCl solution (the coagulate must not dissolve in *cold* soda or HCl solution!), and the liquid submitted to the ordinary tests for albumin. If the coagula consisted of fibrin, these tests will be positive.

Hæmoglobin (*Methæmoglobin*)—*Hæmaturia, Hæmoglobinuria.* In *hæmaturia* the blood enters the urine somewhere in the urinary passages; it may be the result of acute inflammatory affections, neoplasms, or trauma of the kidneys, ureters, bladder, or urethra.

In *hæmoglobinuria* blood pigment that is already in solution in the renal blood passes through the renal epithelia into the urine; hæmoglobinuria may be the result of poisoning (potassium chlorate, mushrooms, sulphureted hydrogen, arseniated hydrogen, pyrogallic acid, etc.); it may also follow the transfusion of blood from one species to another; it may follow severe cutaneous burns and certain infectious diseases. Finally, there is an independent form of paroxysmal hæmoglobinuria of unknown etiology.

In hæmoglobinuria the filtered urine is always red, whereas in hæmaturia, provided the urine is fresh, the filtrate may be colorless. Other substances than blood pigment may, however, impart a red color to the urine so that recourse must be had to one of the following tests in order to establish the presence of hæmoglobin in the urine. (For the detection of blood corpuscles in the sediment see below.)

Tests. 1. Boiling.—In the presence of blood pigment a brown coagulate forms that usually floats on the surface of the liquid and that can be decolorized by shaking the urine with sulphuric acid-alcohol.

2. Heller's Test.—This test is based on the formation of hæmochromogen from hæmoglobin by the action of caustic alkali. Five drops of a ten-per-cent. sodium hydrate solution are added to half a test tube of urine. The mixture is boiled and allowed to stand. The earthy phosphates and carbonates in the precipitate will be found colored brown, brown-red, or blood-red (hæmochromogen spectrum). In alkaline urine the test may fail because the phosphates are already precipitated; to such urine an equal volume of normal acid urine may be added in order to obtain the reaction.

3. Almén's Test.—To 10 c.c. of urine is added a mixture of 5 c.c. of *old* oil of turpentine, and 5 c.c. of tincture of guaiac. If blood pigment is present, a white ring will form that gradually turns blue. The test may be modified by adding 5 c.c. of ether and shaking the mixture; the ether dissolves the pigment and forms a blue layer on top of the urine.

4. Teichmann's Test.—The precipitate obtained in tests 1 or 2, or, better still, the precipitate obtained by the addition to the urine of tannin solution, is filtered off, washed with water and allowed to dry in the air. A small portion is placed on a slide with a crystal of sodium chloride and a drop of glacial acetic acid, covered with a cover slip and heated to boiling for about one minute, the evaporating fluid being constantly replaced by glacial acetic acid, drop by drop. As soon as the fluid turns brown, it is allowed to cool slowly. Under the microscope *hæmin* crystals (Teichmann's crystals, Fig. 4855) of characteristic form and arrangement will be seen.

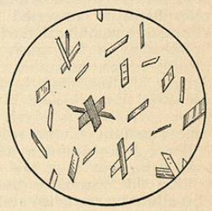

FIG. 4855.—Teichmann's Crystals.

5. Spectroscopic Test.—The diluted urine on direct spectroscopic examination gives the spectrum either of oxyhæmoglobin or of methæmoglobin, provided the urine is acid. On addition of ammonium sulphide the spectrum of gas-free, reduced hæmoglobin appears. After treating the urine with caustic alkali (see Test 2) the spectrum of hæmochromogen appears.

"*Bence-Jones Albumin.*"—This body occurs in the urine in association with multiple myomata of the bones. Nothing is known of its origin. It may be formed in the intestinal tract by some perverted process of disassimilation. This albumin is usually considered an albumose, but it differs from all other known digestive albumoses. It, moreover, resembles true albumin inasmuch as it coagulates on heating to 100° C. (Magnus-Levy), and yields primary and secondary albumoses on peptic digestion. No hetero group can, however, be demonstrated among the digestive products. The body has been found crystallized in the urine.

Test. If urine gives a marked albumose reaction (see above), the presence of Bence-Jones albumin may be suspected, for only in "Bence-Jones albumosuria" do we find such large quantities of "albumose." Such urine should be treated with an equal volume of saturated ammonium-sulphate solution—in this way the body is salted out. It can be further identified by submitting it

to peptic digestion and determining the absence of heteroalbumose and the presence of proto-albumose in the mixture of digestive products.

Histon and Nucleo-Histon.—These two albumins are derived from the cell nuclei; they occasionally appear in the urine in affections accompanied by great destruction of leucocytes.

Test. The urine is freed from albumin by boiling, cooled, and precipitated with four volumes of alcohol (95 per cent.). The precipitate is dissolved in hot water and the solution allowed to cool. In order to get rid of uric acid it is acidified with HCl and allowed to stand for four hours; the uric-acid crystals are filtered off and the filtrate precipitated with ammonia; the precipitate is then washed with water containing a little ammonia and redissolved in diluted acetic acid. This solution, if histon is present, should coagulate on boiling and give the biuret reaction.

NITROGENOUS CONSTITUENTS OTHER THAN ALBUMINS.—From eighty-three to ninety-three per cent. of the urinary nitrogen is secreted as urea; the remaining seven to seventeen per cent. of nitrogen appears in the urine in the form of diamins, amido acids, urea, purin bodies (uric acid and its congeners), nucleinic acid, creatin and creatinin, oxaluric acid, allantoin, preformed ammonia, etc.

The Total Nitrogen and Nitrogenous Equilibrium.—We speak of nitrogenous equilibrium when the output of nitrogen corresponds to the intake. The level of nitrogenous equilibrium varies in different persons and in one and the same individual at different times. It is dependent on the health of the subject, the mode of life, the composition of the food, etc. The following rules govern the level of nitrogenous equilibrium: If an individual is fed on a constant diet sufficiently abundant to maintain full nutrition, then the urinary N-excretion becomes constant at the expiration of from two to four days. The organism, however, has a tendency to accommodate the N-output to the N-intake; and the N-output of one period of twenty-four hours is dependent on the N-intake of the preceding period of twenty-four hours. If the N-intake is altered, the latter factor chiefly determines the N-output in the beginning; after the expiration of a number of days, however, the determining influence of the former factor predominates. If, therefore, the N-intake fluctuates from day to day, the sum of the N-output during a prolonged period of time will equal the sum of the N-intake during this time; but for individual periods of twenty-four hours during this time great differences in the N-output will become apparent. It is clear, therefore, that any calculation in regard to the relation between N-intake and N-output that is based on an observation extending only over a period of twenty-four hours is altogether devoid of value.

A healthy adult can maintain N-equilibrium on 0.6 gm. of albumin per kilogram body weight pro die—or with more. As soon as less N is ingested, N-equilibrium can no longer be maintained, for the organism then begins to disassimilate its proper tissues in order to cover the deficit. The *upper* boundary of N-disassimilation has so far not been determined.

Determination of Total Urinary Nitrogen.—Considerable N is eliminated in the fæces; this N is in part derived from the gastro-intestinal secretions, in part from desquamating epithelia, and in part from ingesta that are not absorbed. This amount of N must be included in the calculation, and must be determined in metabolic studies. N-equilibrium is only established when Food-N *minus* Fæces-N *equals* Urine-N.

The urine should be gathered from morning (before breakfast) to the following morning, not from night to night. The N found in such urine correctly indicates the total N excreted in twenty-four hours: (*a*) if the last nitrogenous food is ingested at least eight or ten hours prior to the collection of the last urine (hence the advantage of collecting from morning to morning); (*b*) if no great fluctuations are permitted in the amount of water ingested during the period of observation as against previous periods; for abundant water-drinking washes out an abnormal amount of nitrogenous material, whereas restriction of fluids exercises the reverse effect and favors the retention of nitrogenous material.

The Kjeldahl Method for Determining the Urinary N.—This method is simpler than all other methods for determining nitrogen; it is more rapid and does not require so much skill and experience on the part of the operator. The method is based on the following principle: The nitrogenous substances of the urine on boiling with concentrated sulphuric acid are destroyed and all the nitrogen that is not in direct combination with oxygen is converted into ammonia, and hence is present in the solution as ammonium sulphate. If the acid solution is now treated with hot soda lye, the ammonia is liberated; it is distilled into a measured quantity of normal acid and the excess of acid titrated back.

According to the concentration of the urine 5 c.c. or 10 c.c. of urine are poured into a so-called Kjeldahl flask (*i.e.*, a flask of hard glass with a round bottom and a long neck, holding from 200 to 300 c.c.); to this are added 20 c.c. of concentrated H_2SO_4, and a small quantity (about one-third gram) of the yellow oxide of mercury. The mixture is boiled until the solution becomes quite colorless, care being taken not to heat too rapidly in order to prevent the escape of vapors. On cooling, the contents of the Kjeldahl flask is transferred to a Kjeldahl retort by repeated rinsing with a little distilled water. The Kjeldahl retort is a large round-bottomed flask holding about 500 c.c. To the liquid in this retort are added 40 c.c., of a solution of sodium sulphide (40 gm. to 1,000 c.c. of water), 160 c.c. of sodium hydrate solution (270 gm. to 1,000 c.c. of water), and a small quantity of talcum. The sulphide is necessary in order to decompose the amido-compounds of mercury that form and that would not give up all their nitrogen if sodium hydrate alone were used. The talcum is added in order to render ebullition more gentle and to prevent bumping. As soon as all the solutions have been poured into the retort it is immediately connected with a condenser and the distillation begun. The vapors of ammonia and the water are collected in a flask containing 40 c.c. of a one-fourth normal H_2SO_4; the distillation is continued until about two-thirds of the fluid have gone over; the condenser is then rinsed with water and the washings added to the distillate. The acid is now retitrated with a one-fourth normal sodium hydrate solution, using rosolic acid as an indicator. The difference indicates the amount of acid neutralized by the ammonia. As 1 c.c. of the one-fourth normal solution represents 0.0035 gm. of N, this figure must be multiplied by the number of cubic centimetres of urine (5 or 10) used for the analysis in order to determine the amount of N contained in this quantity of urine. The N in the twenty-four hours' urine can easily be calculated from this. There are numerous modifications of the Kjeldahl method, but the above plan has been found quite satisfactory and altogether reliable in the hands of the author. (For these modifications and for certain refinements of the methods I refer to Huppert: "Analyse des Harns," 1898, pp. 801 to 807).

Diamins.—The diamins (putrescin and cadaverin) are of rare occurrence in the urine of man and are of subordinate clinical importance.

Amido Acids.—Of this group of nitrogenous urine bodies *carbamic acid* is occasionally found in normal urine, but it has no clinical significance. It is too rare, moreover, to merit discussion in this condensed article. Other members of this group—viz., cystin, leucin, and tyrosin—frequently appear in the urine in crystallized form; they will hence be discussed in detail under the heading of urinary sediments (see below).

Urea.—The excretion of urea is dependent on two factors, viz.: (1) the ingestion of nitrogenous food (chiefly albumins); (2) the catabolism of the organized albumin of the body. As the latter factor is a minor source of urea, and as it is, moreover, fairly constant, the excretion of urea may be said to be largely dependent on the inges-