SO_4, or H_2SO_4 by multiplying the weight of the barium sulphate by 0.3428, 0.4113, or 0.4199.

Determination of Conjugate Sulphates (*Baumann*).—The preformed sulphates are precipitated by barium chloride in the urine after it has been acidified by acetic acid. In the filtrate the conjugate sulphates are then determined.

Fifty cubic centimetres of urine are rendered acid with acetic acid, diluted one-half and precipitated with barium chloride in excess, heated on the water-bath until the barium sulphate settles at the bottom of the vessel, and filtered. The filtrate and washings are then treated as above, *i.e.*, the conjugate sulphates decomposed with HCl and the liberated sulphate determined as barium sulphate. By subtracting the value obtained for conjugate sulphates from the value obtained from the determination of the total sulphates the amount of preformed sulphates can be estimated.

Determination of Preformed Sulphates Directly.—As the barium sulphate precipitate obtained from the original urine often contains phosphates and oxalates, it cannot be weighed directly. In order to get rid of these impurities the precipitate must be repeatedly treated with HCl in a platinum crucible. The procedure is very tedious and is superfluous in view of the fact that the preformed sulphates can be estimated from the difference between total and conjugate sulphates with less trouble. They can also be determined directly by *titration* as follows:

Method of Freund.—Fifty cubic centimetres of urine are treated with ten drops of alizarin red. This colors the urine red. Then five-per-cent. acetic acid is added drop by drop until the red color disappears. When this point is reached, 5 c.c. more of acetic acid are added. The urine is then heated almost to boiling and barium acetate solution added until the liquid again turns red. The solutions required for this estimation are:

(1) A solution of 9.579 gm. of anhydrous barium acetate in 1,000 c.c. of water; 24 c.c. of this solution should correspond to 0.2101 gm. of $BaSO_4$.

(2) Five-per-cent. acetic acid.

(3) One-per-cent. solution of sodium alizarin monosulphate ("alizarin red").

As it is known that 24 c.c. of the barium solution correspond to 0.2101 gm. of $BaSO_4$, the calculation of the preformed sulphates in the 50 c.c. of urine employed in the analysis is simple.

The "Neutral Sulphur" (synonym: suboxidized sulphur, organic sulphur).—Some twelve to fifteen per cent. of the total sulphur of the urine consists of a number of bodies of which we know relatively little; among them are thiosulphates, sulphocyanides, and derivatives of taurin and cystin. A portion of these bodies is readily oxidized, whereas another portion is not oxidized so easily; the former can therefore be converted into sulphuric acid by chlorine or bromine water, the latter require fusing with nitre and potassium hydrate. Cystin belongs to the last-named group of bodies, also taurin, whereas the thiosulphates and rhodanates (sulphocyanides) belong to the former group. The quantity of neutral sulphur compounds is dependent on the quantity and the character of the albumins that are disintegrated in the organism. The neutral sulphur is increased after violent muscular exercise, after a long period of starving, in asphyxia, in chloroform narcosis, after the administration of chloral and of sodium carbonate and sodium citrate (Jawein). After the ingestion of sublimed sulphur a portion of this sulphur reappears in the urine as neutral sulphur. In icterus the neutral sulphur is increased from four to five times above normal (sixty-two per cent., Lépine). In pneumonia the neutral sulphur has also been found increased. In hepatic disorders the compounds that are hard to oxidize seem to be increased, whereas in pneumonia the compounds that are readily oxidizable are increased.

In *cystinuria* a peculiar urinary anomaly characterized by the excretion of cystin, the excretion of neutral sulphur is greatly increased (23.4 to 45.7 per cent.). In addition to cystin certain diamins (putrescin, cadaverin) are found in the urine, and as the disease seems to occur in families, and may persist for a lifetime, we are probably dealing with a peculiar metabolic anomaly in which the oxidation of the albumins is perverted. Some authors (v. Jaksch) are inclined to attribute cystinuria to a particular form of intestinal mycosis. I consider the former view more plausible. The disease is very rare. The chief clinical significance of the urinary excretion of cystin is the tendency to calculus formation that is thereby created. The appearance of cystin in the urine should always constitute a warning of impending cystin gravel or calculi. (See also Urinary Sediments.)

Tests for Neutral Sulphur.—The total sulphuric acid is first precipitated by hydrochloric acid and barium chloride, as explained above, the excess of barium removed from the filtrate by soda, the filtrate evaporated to dryness, the residue fused with nitre (and soda), the solution of this fused mixture treated with barium chloride, and the sulphuric acid precipitated. To determine the presence of sulphur that is readily oxidized the filtrate of the urine after removal of the total sulphuric acid, as above, is acidulated and treated with bromine; on addition of barium chloride any sulphuric acid formed by this mild oxidation will be precipitated.

The qualitative tests for thiosulphates and sulphocyanides will not be given in this article, because the clinical significance of these bodies is too subordinate.

The quantitative estimation of the neutral sulphur is performed according to the same principles as the qualitative tests for this group of bodies. The urine may first be oxidized and the total sulphur determined; then the total performed and conjugate sulphates may be determined separately and the quantity of the neutral sulphur calculated from the difference. In order to determine the total sulphur by oxidation a measured quantity of the urine is evaporated to dryness and the residue glowed with a fusing mixture consisting of four parts of nitre and one part of soda. The white ash is treated with hydrochloric acid and evaporated to dryness, this process being repeated three or four times in order to get rid of all the nitric acid. The residue is then dissolved in water and the sulphuric acid determined as described above. Other methods of oxidation, *i.e.*, with nitric acid (Mohr), with sodium superoxide (Clark), will not be described, as they possess no advantages over the oxidation with nitre soda.

Cystin may be precipitated from the urine by benzoyl chloride, and the sulphur determined in the precipitate. Two hundred cubic centimetres of the urine are treated with 10 c.c. of benzoyl chloride and 70 c.c. of a ten-per-cent. sodium hydrate solution and shaken until the odor of benzoyl chloride disappears. The precipitate consists of benzoyl cystin and can be used directly for a sulphur determination by oxidation. The presence of cystin in the benzoyl chloride precipitate is made probable if a black sediment forms when the precipitate is boiled with a solution of lead oxide in soda lye. The black sediment consists of lead sulphide, and consequently also denotes the presence of sulphur.

Sulphureted Hydrogen.—Sulphur may finally occur in the form of sulphureted hydrogen. Fresh urine rarely contains H_2S or sulphides, but nearly every old urine emits an odor of H_2S when treated with mineral acids. Hydrogen sulphide does not appear in the urine in diseases that are accompanied by putrefactive processes, nor does it appear after the ingestion of alkali sulphides, nor after sulphur baths. Occasionally H_2S passes into the bladder from the rectum if some abnormal communication exists between these two viscera. Certain bacteria may infect the bladder and may lead to the generation of H_2S in this viscus.

Tests.—The urine should of course be fresh. The *odor* may be characteristic. Lead acetate may form a black precipitate of lead sulphide. A piece of paper may be saturated with a solution of lead acetate, the urine poured into a bottle, and a current of air forced through the liquid. The lead paper is held over the neck of the bottle. If H_2S is driven off, the paper will turn brown

or black. Quantitative determinations of H_2S in urine are clinically without value.

Phosphoric Acid (*Phosphates*).—The urine always contains phosphoric acid; the average daily excretion is 3.5 gm. of P_2O_5; the quantity is largely dependent on the character of the diet; increased catabolism of cell nuclein either of the food or of the proper tissues causes an increase of phosphoric acid.

Four phosphates appear in the urine, viz.: (1) NaH_2PO_4 = monosodium phosphate; (2) Na_2HPO_4 = disodium phosphate; (3) Na_3PO_4 = trisodium phosphate; (4) Na_3PO_4 (+NaOH) = basic sodium phosphate. (1), (2), and (3) are also called the acid, neutral, and basic phosphate respectively; (4) would then be "overbasic." Some writers speak of (1), (2), and (3) as primary, secondary, and tertiary phosphate. The designation adopted above is the most popular and the most rational one.

The monophosphates can be converted into the di- and triphosphates by the addition to the urine of alkali hydrates or carbonates. Inversely the tri- and diphosphates can be converted into monophosphates by acids.

Tests. In acid urine the addition of ammonia at once produces a precipitate of earthy phosphates. The filtrate contains normal alkali phosphate. The latter when treated with magnesia mixture gives a precipitate of triple phosphate; or the filtrate may be acidulated with acetic acid and tested for phosphoric acid with uranium nitrate or ferric chloride. The former produces a yellowish-white precipitate, the latter a white precipitate that stains yellow with an excess of ferric chloride solution. For the analysis of phosphatic sediments see below under Urinary Sediments.

Sometimes it is necessary to get rid of the urinary phosphates prior to undertaking certain other tests. For this purpose the urine is precipitated with neutral or basic lead acetate, or the urinary phosphates are converted into normal phosphates by treating the urine with alkali hydrate and the solution precipitated with some calcium or barium salt. The filtrate will be free from phosphates.

Quantitative Estimation. Solutions.—(1) Solution of uranium nitrate containing 35.461 gm. of the salt to a litre. Uranium nitrate is dissolved in a little less than 1,000 c.c. of water and titrated against a solution of disodium phosphate (10.0845 gm. of $Na_2HPO_4.12H_2O$ to 1 litre), 50 c.c. of which should correspond to 0.1 gm. of P_2O_5. In order to bind the nitric acid developed in this titration, 3 gm. of sodium acetate are added to the uranium nitrate solution. The results of the titration indicate how much the uranium nitrate solution must be diluted to correspond to the phosphate solution.

(2) A solution of 100 gm. of sodium acetate and 30 gm. of acetic acid to a litre, 5 c.c. of this mixture are used for every 5 c.c. of urine. The solution contains enough acetic acid to convert all the urinary phosphates into monophosphate.

(3) Tincture of cochineal to be used as an indicator, 5 gm. of cochineal are dissolved in the cold in 500 c.c. of a mixture of 4 parts of water and 1 part of alcohol. Any undissolved residue is removed by filtration.

The uranium solution is now standardized; 20 c.c. should exactly neutralize 50 c.c. of the phosphate solution; 50 c.c. of the latter solution are mixed with 5 c.c. of the acetate solution (2) and a few drops of the indicator (3) added. The mixture is heated to boiling and uranium solution added, drop by drop. The appearance and persistence of a green-colored precipitate indicates the end reaction. If in this titration only 18 c.c. of uranium solution were required to neutralize the 50 c.c. of phosphate, then the uranium nitrate solution must be diluted so that 2 c.c. of water are added to every 18 c.c. of the solution.

Execution: Fifty cubic centimetres of urine are treated exactly as the 50 c.c. of phosphate solution above. As 20 c.c. of the uranium nitrate solution correspond to 50 c.c. of the phosphate solution, and as these 50 c.c. represent exactly 0.1 gm. of P_2O_5, the phosphate content of the urine can be estimated by simple calculation from the number of cubic centimetres of the uranium solution required to bring about the end reaction in 50 c.c. of urine.

The separate estimation of the different phosphates cannot be discussed in this place. (I refer to Huppert, "Harnanalyse," p. 734 *ff.*, 1898.)

Carbonic Acid (*Carbonates*).—The urine may contain free carbonic-acid gas or carbonic acid combined with various bases as carbonates. Free carbonic acid can be driven off by physical means (boiling, passage of an air current, evacuation); the latter can only be removed by chemical means (acids). The proportion of the former to the latter is about as two to one. Normal urine of the specific gravity of 1.020 and of acid reaction on an average contains about 50 c.c. of free carbonic acid; urine of an alkaline reaction over 100 c.c. of carbonic acid. As the salts of vegetable acids appear in the urine as carbonates, a vegetable diet (citrates, acetates, tartrates, etc.) leads to an increased excretion of carbonates.

An important interrelationship exists between the free CO_2, the carbonates, and the phosphates of the urine. Monosodium phosphate liberates CO_2 from alkali carbonates. If the free CO_2 developed in this way is removed, more alkali carbonate is disassociated until finally only traces of it are left. Carbonic acid forms mono-(acid) and di-(normal) carbonates ($NaHCO_3$ and Na_2CO_3). The urine may contain the carbonates of Ca, Mg, and NH_3.

Tests. A current of air is passed through an alkali hydrate solution (to remove any CO_2 it may contain), then through the urine, and finally through a solution of barium hydrate (baryta water). The presence of CO_2 will be revealed by clouding of the barium solution. Fixed alkali carbonates must first be disassociated by treating the urine with mineral acids.

Quantitative Estimation. This is performed in the same way as the qualitative test. The vessel containing the baryta solution is weighed before and after; the difference represents the CO_2 absorbed. For details I refer to text-books of analytical chemistry.

Silicic Acid (*Silicates*), *Nitrates* and *Nitrites*, and *Hydrogen Peroxide* are all occasionally encountered in traces in human urine. The silicates, nitrates, and nitrites are derived from the ingesta, probably from drinking water that always contains all these bodies. The source and significance of the traces of H_2O_2 that are occasionally found are not understood. None of these substances have sufficient clinical importance to warrant a description of their properties, nor of the methods employed for their detection and estimation in the urine.

Bases.—The bases normally occurring in the urine have been in part discussed under the headings of chlorides, sulphates, phosphates, etc. For the exact quantitative determinations of K, Na, Ca, Mg, and Fe, that are of great scientific interest in metabolic work, but only of subordinate, practical, *i.e.*, clinical interest, I refer to text-books of quantitative chemical analysis. The quantitative determination of *ammonia* alone is of sufficient practical importance, however, to warrant description in this article (see below).

The bases of the urine can be conveniently discussed in groups (Na and K, Ca and Mg, NH_3, Fe). The facts given under acids (and salts) may be supplemented by the following information:

Potassium and Sodium.—The urine voided in twenty-four hours by a healthy adult contains from 2 to 4 gm. of potassium (K_2O) and from 4 to 8 gm. of sodium (Na_2O). The excretion of Na and K is largely dependent on the character of the diet. During inanition their quantity is reduced and more K is excreted than N. As soon as food is taken, the excretion increases only slowly and the normal proportion between Na and K is soon reestablished. Vegetable K salts increase the Na excretion. Muscular exercise increases the K excretion. In fever the K excretion may be doubled or trebled and the Na excretion be greatly reduced. As soon as the fever disappears the Na excretion rises and the K excretion falls (Salkowski). These peculiar fluctuations may, I think, in large part be explained by the small ingestion of

food (containing NaCl) during fever and the increased feeding during convalescence.

Tests. Sodium.—The urine is evaporated to dryness. The residue held in a colorless flame colors it yellow. Spectroscopically an absorption line at D.

Potassium.—One hundred cubic centimetres of urine are acidified with HCl, and treated with a mixture of equal parts of alcohol and ether containing platinum chloride. In the course of three to four hours octahedric crystals of K platinum chloride from a yellow precipitate that presents characteristic microscopic features.

Calcium and Magnesium.—The average daily excretion of Ca(CaO) is from 0.2 to 0.3 gm., of Mg(MgO) from 0.1 to 0.25. Only a small proportion of the Ca absorbed from the intestine is excreted in the urine (five to fifteen per cent.); the greater portion passes into the bowel. Abundant water drinking increases the urinary Ca excretion. During inanition there is a slight increase in the Ca excretion (probably derived from osseous tissues). In osteomalacia the Ca excretion is increased; in rachitis it is not increased. The writer has shown that in tuberculosis the Ca excretion is often increased.

Tests. If the urine is treated with ammonia the precipitate that forms consists largely of Ca phosphate and Am- Mg phosphate. In order to demonstrate the presence separately of Ca and Mg the precipitate (or the sediment of alkaline urine) is dissolved in acetic acid, the solution treated with ammonium chloride and a solution of ammonium oxalate. The Ca is precipitated as Ca oxalate, while Mg remains in solution. By adding ammonia to the filtrate, Mg can again be precipitated as Am- Mg phosphate.

Ammonia.—The normal daily excretion of Am is from 0.3 to 1.2 gm. The urinary Am constitutes from 4.5 to 7 per cent. of the total N. On an abundant meat diet more Am is excreted than on a vegetable diet. As urine readily undergoes ammoniacal fermentation the urine should be examined fresh. Fixed alkalies and vegetable alkalies (that are excreted as carbonates) decrease the Am excretion, inorganic alkali salts increase it. Ammonia salts (carbonate and vegetable salts) appear in the urine as urea. As urea is formed from Am carbonate in the liver, the Am excretion (both absolutely and in proportion to urea) is increased in advanced affections of the liver (interstitial hepatitis, etc.). In amyloid liver and in splenic leukæmia the Am excretion is increased. Inorganic acids lead to an increased excretion of Am. Acidosis of the blood from whatever cause also increases the urinary Am. Asphyxia, febrile conditions with high temperatures, diabetes, phosphorus poisoning—all lead to an increased Am excretion, and this phenomenon can readily be explained either on the basis of acidosis or impairment of the liver function. Excessive Am excretion has been observed in the algid stage of cholera (2.075 [!] Rumpf).

Qualitative Test. As urea is readily converted into Am carbonate by micro-organisms the urine must be quite fresh. The urine is rendered alkaline with lime water. Am escapes and colors red litmus paper blue. KOH and NaOH cannot be used in this test because they may liberate Am from other nitrogenous bodies of the urine than Am salts. The precipitate of K platinum chloride described under Potassium may be treated with NaOH; it will also emit vapors of Am that can be recognized as above.

Quantitative Tests. The most popular method is that of Schlösing; it is not quite accurate and it has frequently been modified in minor details. The original method is, however, so simple of execution, and requires so little paraphernalia, that it is best suited for clinical work. The methods of Wurster (distillation), of Heintz, and of Schmiedeberg (determination as Am platinum chloride) are all good. I refer to Huppert, "Harnanalyse," 1898, p. 743 *ff.*, for details.

The Method of Schlösing. Twenty-five cubic centimetres of filtered urine are poured into a shallow crystallizing dish; upon this is placed a metal triangle that serves to support a second flat dish containing 20 c.c. of one-fourth normal H_2SO_4. To the urine are added 10 c.c. of lime water. The two vessels are at once covered with a bell jar with ground edge that is greased; it is pressed tightly down upon a ground glass plate. After three or four days all the ammonia is driven out of the urine and is absorbed by the sulphuric acid. The acid is then titrated back with one-tenth normal sodium hydrate solution, using methyl orange as an indicator. The ammonia absorbed by the acid, *i.e.*, originally contained in the urine, can readily be calculated from the number of cubic centimetres of the alkaline solution required to neutralize the free acid remaining. (The number of cubic centimetres of one-tenth normal NaOH may be subtracted from 50 and multiplied by 1.7 to indicate the milligrams of NH_3 found).

Iron.—Iron occurs in the urine only in organic combinations; hence its presence can only be demonstrated in the urinary ash. The uric-acid crystals of the urine usually contain some of the iron. The color of the uric-acid crystals is not, however, due to the traces of iron they may incorporate. The nature of the organic iron compound of the urine is not known. The average daily iron excretion is about 4 mgm. In fever and in pernicious anæmia the urinary iron is increased.

Test. The urinary ash is dissolved in a little HCl and boiled with one drop of nitric acid. After cooling the liquid is treated with potassium sulphocyanide solution. If iron is present even in traces a few drops of this reagent will produce a reddish color; if much iron is present, the liquid will turn dark red. Or the HCl-HNO_3 solution of the ash may be treated with potassium ferrocyanide solution. If iron is present, a blue flocculent precipitate will form.

Accidental Admixtures.—Many drugs and poisons may occasionally appear in the urine. See for this subject the article on *Poisons*.

URINARY SEDIMENTS.

The urine is usually quite clear or only slightly clouded when fresh. On standing, a small nubecula soon forms that, on microscopic examination, is found to consist of a small number of epithelial cells, a few leucocytes, and a scanty number of crystals. The size and the density of this nubecula varies greatly even in health. If the urine is concentrated, large urate precipitates may form in subjects who are perfectly well. Pathologically, many other organized and unorganized morphotic elements may appear in the urine that have great diagnostic significance. Pathologic urines containing many abnormal elements usually precipitate a distinct sediment after standing a short time. In other cases the pathologic constituents may be so scanty that they must be precipitated by centrifugation. If it is desired to preserve the sediment for a time the urine should be treated with chloroform water (5 c.c. to 1 litre). Staining the sediment is rarely necessary. The same methods and the same stains may be used as in other histologic work.

Organized Sediments.

Red Blood Corpuscles.—These elements appear in the urine in extrarenal and renal hæmaturia (see these paragraphs). The cells appear under the microscope as yellow circular discs with a central depression; seen from the side they assume a biscuit form. They soon undergo morphologic changes, and either swell up or shrink and lose their circular contour. They also appear together with white blood corpuscles and can be distinguished from the latter by the absence of a nucleus, their yellowish col-

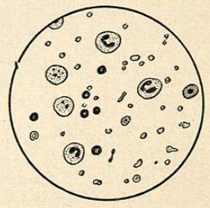
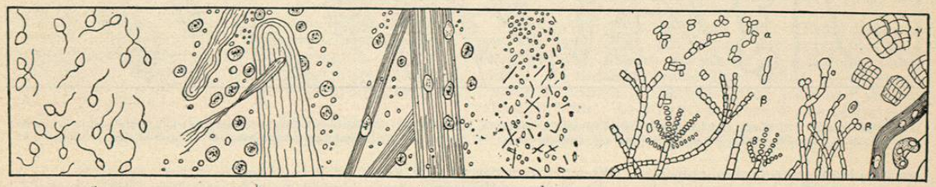


Fig. 4857.—Red and White Blood Corpuscles.

or, the central depression, and their size. (See Figs. 4857 and 4858 *b* and *c*). There are always more red than white cells in simple hæmaturia; in pyuria there are more white than red. Occasionally the pigment is washed out of the red blood corpuscles, and they appear as rings ("shadows").

White Blood Corpuscles (Leucocytes, Pus Cells).—A few leucocytes can always be found in normal urine. They appear as round colorless elements with one or more nuclei and with homogeneous, finely or coarsely granular protoplasm. The smaller leucocytes usually possess only one nucleus and homogeneous protoplasm (see Figs. 4857 and 4858, *b* and *c*). The finer differences can best be brought out with Ehrlich's triple stain, but for ordinary urinary diagnosis this is superfluous. Many degenerated forms are often seen, particularly in alkaline urine. The normal outline may be lost, the cells may be swollen, their protoplasm may be in all stages of fatty, hyaline, or granular degeneration. Sometimes nothing is left of the cells but the nucleus. The greatest number of leucocytes (pus cells) appears in rupture of an abscess into the urinary passages and in cystitis. The pus may be derived from any portion of the uropoietic apparatus. In renal suppuration the number of pus cells is usually small. The localization of the pus focus may occasionally be attempted from the examination of the other formed elements that appear in the urine at the same time (see *Epithelia*). Particular care should be exercised in women, as much pus may come from the genital apparatus. In order to differentiate pus cells from epithelial cells the sediment may be treated with iodic-potassium iodide. The leucocytes will turn mahogany brown (glycogen), while the epithelia will turn light yellow.



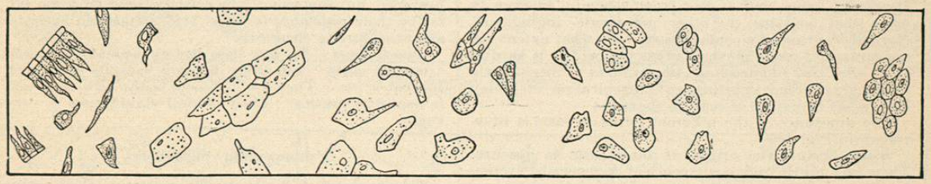
a. *b.* *c.* *d.* *e.* *f.*

Fig. 4858.—*a*, Spermatozoa; *b*, cylindroids, pus (red and white blood corpuscles); *c*, fibrin, red and white blood corpuscles (hæmaturia); *d*, micrococcus ureæ, bacillus ureæ, large bacillus found in cystitis; *e*, yeast (α), penicillium glaucum (β); *f*, oïdium albicans (α), mycelial filaments (β), sarcina (γ). (Original.)

Spermatozoa (Fig. 4858 *a*).—These consist of a head and a tail; the former thick and pear-shaped, the latter thin and filamentous, and becoming attenuated at its distal end. In some cases the spermatozoa are motile. They are about 50 μ long, the head usually being from 4 to 5 μ in length.

Spermatozoa are found after coitus or emissions (epileptic seizures, nocturnal pollutions, etc.) in male urine, and may also occasionally be found in the first urine voided by women after coition.

Parasites.—For pathologic bacteria and for animal parasites I refer to other portions of this work. The urine may contain almost any one of the *pathogenic bacteria*. Particularly common are the gonococcus, the tubercle bacillus, and septic cocci. Of *animal parasites* (vermes) distoma hematobium, filaria sanguinis hominis, echinococcus, eustrongylus gigas, and occasionally ascarides are found in the urine. Various *infusoria* have also been described in the urine. Of non-pathogenic schizomycetes and hyphomycetes and non-pathogenic bacteria (cocci, bacilli, sarcinæ, etc.) a great many have been described. The most important ones of this group are micrococcus ureæ, bacillus ureæ, a long bacillus frequently found in cystitis urine, a sarcina, yeast, penicillium glaucum, oïdium albicans, and mycelia. The appearance of some of these organisms is pictured in Fig. 4858, *d*, *e*, and *f*. Few of them are ever found in fresh urine. They rapidly develop, however, in old urine, particularly in diabetic urine, so that they may form a film or zooglœa on the surface of the liquid. They bring about fermentative changes that have been referred to incidentally in the text above.



a. *b.* *c.* *d.* *e.*

Fig. 4859.—Epithelia. *a*, Male urethra; *b*, vagina; *c*, vesical; *d*, renal; *e*, pelvis and ureter. (Original.)

Epithelia are found in normal urine. Their number, however, is scanty. Occasionally normal urine contains large numbers of round epithelia that are derived from the prepuce in men or the meatus urinarius or the vagina in women. If such epithelia are present in very large number, this finding usually denotes catarrh of these parts. It is a very difficult matter to differentiate the epithelia of the kidneys, the pelvis, ureters, bladder, and urethra. As a rule, although not always, *renal epithelia* are smaller than the epithelia from lower portions of the urinary tract. They have a large oval nucleus, a polyhedric outline, and granular protoplasm. They may be single or arranged in groups. If cells possessing all the above characteristics are found arranged in cylinders (see also *Casts*) the diagnosis of renal epithelium is justified. The renal cells may be in all stages of degeneration, and occasionally a tentative diagnosis of the character of the renal epithelium may be permitted from the appearance of these cells. *Pelvis cells* are usually elongated with a thick rounded end containing a nucleus and a longer attenuated extremity (Fig. 4859, *e*). I never attach much importance to cells of this appearance, for I believe that they can be derived from the kidneys or the ureters as well, for the epithelia lining these portions of the urinary passages are after all of the same type, and any morpho-

logical differences that may occasionally be observed are probably accidental. Large islands of squamous epithelium speak for cystitis. In men they are in all probability derived from the bladder mucosa; in women they

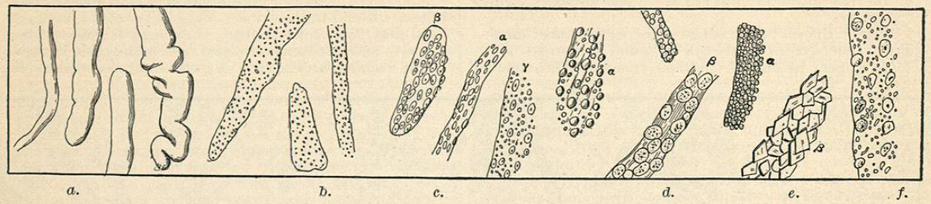


FIG. 4860.—Casts. *a*, Waxy and hyaline casts; *b*, granular casts; *c*, blood casts; (α) red blood-corpuscle cast; (β) leucocyte cast; (γ) mixed blood cast; *d*, (α) fat casts; (β) epithelial cast; *e*, pseudo-casts; (α) urate cast; (β) dicalcium phosphate cast; *f*, mixed cast. (Original.)

may be bladder or vaginal epithelia. When we consider finally that all these epithelial cells may be and usually are degenerated and consequently changed in outline and appearance, we should be warned not to place too great diagnostic importance on slight morphologic differences they may present. Fig. 4859 illustrates in a diagrammatic manner the different forms of urinary epithelia.

CASTS.—Urinary casts or urinary cylinders are clinically the most important morphotic elements of the urine. We can distinguish organized casts and unorganized casts, the former consisting of morphotic elements or the products of their metamorphosis (*scil.* degeneration), the latter consisting of crystals of inorganic urinary constituents. Some writers class the latter as *pseudo-casts*, and include under the category of casts proper only the former. I consider this differentiation to be more useful from the clinical standpoint.

Casts proper may again conveniently be subdivided into homogeneous (waxy, hyaline) casts, cell casts (epithelial, blood, etc., casts), and casts consisting of formed degenerated cell products (fatty, granular, etc., casts). Often we encounter *mixed casts*, *i.e.*, for instance a homogeneous cast with cellular elements and degeneration products and frequently crystals besides. Bacterial casts are also occasionally seen. All classification of casts is more or less artificial and serves no real purpose.

Casts may appear in varying numbers. They may appear in urine that is free from albumin, or even in urine that contains no other pathologic ingredients. Normal (?) urine may contain casts. To what extent the appearance of casts is ever "physiological" it is hard to say. (See also *Physiological Albuminuria*.) Slight toxic influences (alcohol, intestinal auto-intoxication, etc.) may lead to the excretion of casts in the urine.

The appearace of the different forms of casts is illustrated in Fig. 4860.

Waxy Casts.—The origin of these casts is obscure. They may result from coalescence of degenerated epithelia, from inflammation, from exudation of amyloid or fibrin into the uriniferous tubules. They are usually long, often segmentated, sometimes short and broad (fragments). They may either be smooth or shiny, or may be covered with morphotic elements. They always indicate some renal affection. They appear in acute and chronic nephritis, in amyloid kidney, and in contracted kidney. They occasionally give the amyloid reaction, but not always. A positive amyloid reaction does not necessarily indicate amyloid kidney.

Hyaline Casts.—These structures are usually very long, pale, and very delicate, so that they may readily escape detection. Hyaline casts alone are probably of no pathologic significance, and nephritic lesions should never be diagnosed from their presence alone. Frequently they are covered with morphotic elements that possess pathologic importance.

To the same category probably belong *cylindroids* (Fig. 4860, *b*). These constitute bands and cylinders that are similar in appearance to hyaline casts. They are very common. Occasionally they are found in normal urine. They seem to be a product of slight renal irritation, but their presence by no means indicates a renal lesion proper. They have been found in congestion of the kidney, from heart lesions, and in increased urate excretion.

Blood Casts.—These structures are formed whenever there is hemorrhagic exudation into the canaliculi of the kidney parenchyma. The origin of

Epithelial Casts is equally clear. They are the result of epithelial desquamation that may be due to a great variety of causes.

The presence of blood and epithelial casts always denotes acute nephritis or an acute exacerbation of a chronic nephritis. They are consequently of the greatest diagnostic importance.

Fatty Casts.—Fat droplets are frequently found on granular casts; sometimes casts consisting of fat globules alone are seen. Occasionally fat globules and fat needles (crystals of fatty acids and soaps) appear together. Fatty casts occur only in subacute and chronic forms of nephritis that lead to fatty degeneration of renal parenchyma, *i.e.*, of renal epithelia.

Granular Casts.—These casts probably result from granular degeneration of blood and epithelial casts. They indicate renal inflammation. They occasionally appear in cyanotic induration of the kidney. They usually appear together with the other forms of casts described, and they possess great diagnostic significance.

Bacterial Casts usually indicate embolic septic nephritic processes. They often resemble granular casts in appearance, but can usually be distinguished from the latter by their resistance to nitric acid, potassium hydrate, and other strong chemicals.

Pseudo-Casts.—To this class belong hæmatoidin casts, "detritus casts," and casts holding crystals of urates, sulphates, etc. They are common in the new-born and in nephritis uratica. Their clinical significance is very slight.

UNORGANIZED SEDIMENTS.

The character of the inorganic sediment is dependent on the reaction and the concentration of the urine and on the mixture of salts it contains. Much can be elicited in regard to the sediment from its behavior to heat, the reaction of the urine and its behavior to acids. Thus a red sediment in acid urine that is soluble on heating always denotes uric acid, whereas a white sediment in alkaline urine that is insoluble on heating the urine alone, but readily soluble in warm urine after the addition of a little acid, denotes phosphates (*plus* carbonates and urates). Phosphatic sediments always appear when the urine is alkaline when voided, or becomes alkaline on standing (fermentation). The sediment may be crystalline or amorphous. The composition of the sediment can be determined by microscopical and chemical analysis. Only the most important sediments and the methods employed for their recognition can be discussed in this article.

URIC ACID (see Fig. 4861).—This sediment, as shown

in the drawing, may appear in a great variety of forms. Pure uric acid is white. The urinary uric acid is always colored red to dark brown from the admixture of urinary pigments. The crystals readily dissolve under the microscope on addition of potassium hydrate solution, and reappear in a short time as rhomboid crystals on addition of hydrochloric acid. Uric-acid crystals, as already stated, only occur in acid urine.

URATES.—Alkali urates appear as amorphous fine granules of yellow or reddish-brown color in acid urine, whereas ammonium urate occurs only in alkaline urine in the form of spheres that are surrounded by a wreath of fine needles or spiculæ. The morphologic characteristic of amorphous urates and of ammonium urate are represented in Fig. 4862. Urates are soluble under the microscope on addition of acids. On standing, crystals of uric acid appear.

CALCIUM OXALATE (see Fig. 4863).—These crystals present so typical a microscopical appearance that they

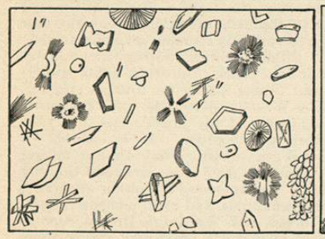


FIG. 4861.—Uric-Acid Sediment. (Original.)

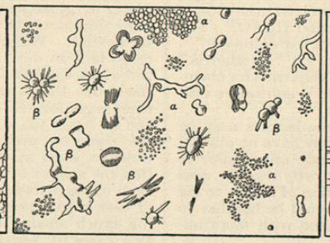


FIG. 4862.—α, Amorphous urates; β, ammonium urate. (Original.)

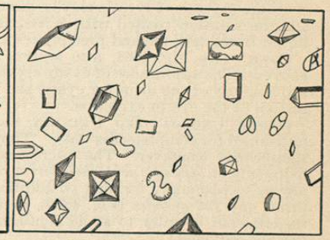


FIG. 4863.—Calcium Oxalate. (Original.)

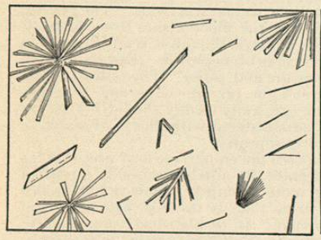


FIG. 4864.—Calcium Sulphate. (Original.)

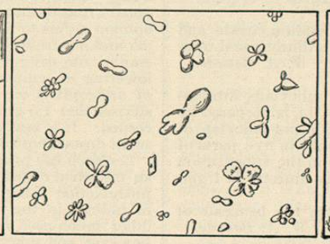


FIG. 4865.—Calcium Carbonate. (Original.)

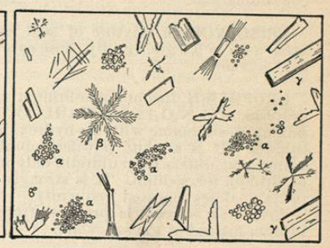


FIG. 4866.—Phosphate Sediments. α, Amorphous earthy phosphates; β trimagnesium phosphate; γ, triple phosphate. (Original.)

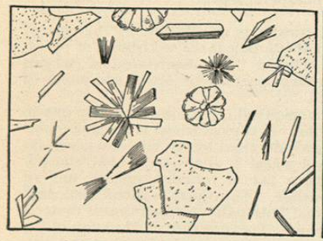


FIG. 4867.—"Neutral" or Dicalcium Phosphate. (Original.)

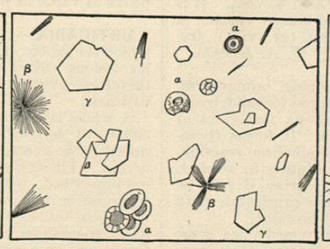


FIG. 4868.—Leucin, Tyrosin and Cystin. α, Leucin; β, tyrosin; γ, cystin. (Original.)

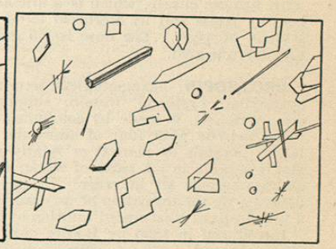


FIG. 4869.—*a*, Hippuric acid; *b*, cholesterin; *c*, fatty crystals; *d*, urea nitrate; *e*, fat globules. (Original.)

cannot be confounded with anything else. They occur in normal urine, and may appear in large numbers after the ingestion of certain vegetables (asparagus, beans, carrots, etc.) that contain oxalic acid. If this factor can be ruled out, the appearance of much calcium oxalate sediment should lead to the chemical estimation of the urinary oxalic acid as described above.

CALCIUM SULPHATE (Fig. 4864).—This is a rare urinary sediment. The crystals are soluble in acids and in ammonia. The pathologic significance of these crystals is small.

CALCIUM CARBONATE (see Fig. 4865) is a rare sediment of subordinate clinical importance. On addition of mineral acids the sediment rapidly dissolves. Under the microscope effervescence can be seen.

PHOSPHATES (Figs. 4866 and 4867).—These salts appear in two forms, amorphous and crystalline. As already stated, alkaline urine always precipitates phosphates. If the urine is acid when voided, increased excretion of phosphates may be taking place and still no sediment form. As a rule, therefore, a phosphate sediment has only slight clinical importance. There is, however, a metabolic disorder that may lead to phosphaturia. We distinguish: (1) Amorphous earthy phosphates (calcium and magnesium phosphate); (2) trimagnesium phosphate; (3) dicalcium phosphate (stellar phosphate); (4) ammonium-magnesium phosphate (triple phosphate). (1)

Occurs in alkaline or neutral urine; (2) in concentrated alkaline urine; (3) in neutral or slightly acid urine containing large quantities of calcium phosphate; (4) chiefly in alkaline urine, particularly after ammoniacal fermentation. It may also occur in feebly acid urine. Needless to say that several of these phosphates may and often do occur together.

Leucin and Tyrosin (see Fig. 4868).—Leucin and tyrosin usually occur together. The microscopical appearance is characteristic. They appear in the urine in acute yellow liver atrophy, in phosphorus poisoning, and in a number of infectious diseases.

Chemically leucin crystals can be recognized by evaporating the crystals with HNO_3 on a piece of platinum foil. A colorless residue remains that forms an oily mass when touched with a solution of KOH.

Tyrosin treated in the same way with HNO_3 forms a yellow residue, that treated with NaOH gives a reddish color. If the mixture is evaporated to dryness a brown-black mass remains.

Or the crystals of tyrosin may be dissolved in hot water and the solution treated with KNO_2 and $HgNO_3$. The liquid turns dark red and precipitates a red sediment.

Cystin (see Fig. 4868, also section on "Cystinuria" above).—The appearance of cystin crystals calls for chemical analysis of the urine for cystin and quantitative estimation of the cystin excretion.

Other Unorganized Urinary Sediments may be mentioned for completeness' sake. They have no clinical significance whatever. The microscopic appearance of sediments of *hippuric acid, cholesterin, fatty crystals, urea nitrate,* occasionally forming on addition of HNO_3 to the urine, and *fat globules* (Fig. 4869), should be familiar to the clinician in order to avoid confusion with more important sediments.

Urinary sediments may also contain xanthin, blood pigment, bile pigment, indigo, and numerous accidental contaminations. *Alfred C. Croftan.*

URISOLVIN is a mixture of acid lithium citrate and urea, used in 0.2 gm. (gr. iij.) dose as a diuretic and uric-acid solvent. *W. A. Bastedo.*

UROPHERIN, theobromine-lithium salicylate, lithium-diuretin, $C_7H_7N_4O_2Li + C_6H_4OH.COOLi$, is prepared by mixing theobromine with the hydroxide and salicylate of lithium. It is a white powder soluble in five parts of water, and differs from diuretin only in the substitution of lithium for sodium. It is strongly diuretic in 1 gm. (gr. xv.) doses repeated frequently.

Uropherin benzoate is prepared from the benzoate of lithium instead of the salicylate. *W. A. Bastedo.*

UROSIN, lithium quinate, is made by mixing quinic acid, which tends to prevent the formation of uric acid, with lithium citrate, which is a uric-acid solvent. It is held by Weiss and by Sternfeld to be almost specific in attacks of gout. The dose is 0.5 gm. (gr. viij.), frequently repeated. *W. A. Bastedo.*

UROTROPIN, hexamethylene-tetramine, aminoform, cystamine, cystogen, formin, ammonio-formaldehyde, etc., $(CH_2)_6N_4$, is made by combining six molecules of formaldehyde with four of ammonia. It forms rhomboidal crystals of neutral or faintly alkaline reaction, and is soluble in 1.2 parts of water, slightly in alcohol, and scarcely at all in ether. In the urine it may be detected by the formation of an orange precipitate with a few drops of a saturated solution of bromine.

Introduced in 1895 by Bordet, this remedy has come into universal use as a urinary antiseptic. It is very rapidly absorbed, Casper finding it in the urine in ten minutes; usually the urine continued to give off formaldehyde for several days. In a few cases no formaldehyde was demonstrable though urotropin was constantly excreted, and Citron calls attention to the fact that formaldehyde is sometimes not liberated in strongly alkaline urine. The blood of a rabbit, to which Casper administered urotropin hypodermically, was shown to contain formaldehyde.

The drug has been recommended as a diuretic, a uric-acid solvent, and a urinary antiseptic and acidifier. Thompson considers its diuretic powers to be very slight, though other observers report considerable increase in the flow of urine following large doses. As a uric-acid solvent Casper found that neither a urotropin solution nor the urine of a patient taking urotropin had any effect *in vitro.* He discovered accidentally, however, that it caused complete cessation of all visible phosphate excretion in a case of phosphaturia.

It is in bacterial conditions of the urine, however, that urotropin finds its chief indication. In typhoid fever there is much evidence that the bacilli are prevented from developing in the urine; at Johns Hopkins Hospital the typhoid bacilli did not completely disappear from the urine, but were much diminished in numbers. Osler recommended the drug very highly in typhoid cystitis. In suppurative pyelitis and cystitis urotropin has the power of greatly lessening bacterial action, while at the same time it tends to diminish the alkalinity or increase the acidity. When the urine is strongly alkaline it sometimes fails to act. Cohn found no improvement in tuberculous cystitis or in cystitis following acute gonorrhœa, but Bangs and others advise its routine employment in gonorrhœa, as it tends to keep the urine antiseptic and to lessen the tendency of the gonococcus to invade the posterior urethra and bladder. A. R. Elliott, of Chicago, gives up to 6 gm. (ʒ iss.) a day, though noting that the acidity of the urine may be so increased thereby as to cause irritation. But there are a number of reports of vesical irritation, hæmaturia, and even melæna following much smaller doses. W. Langdon Brown reports two cases of vesical hæmaturia from ten grains three times a day for eight days. Morton noted burning in the urethra and frequent micturition from twenty-four grains a day. Biss, in three hundred and eleven typhoid cases, noted irritation and slight hæmaturia twice. The general opinion seems to be that the blood comes from the bladder and not from the kidneys, though it is advised not to employ the drug in cases of nephritis. Eastman noted lowering of temperature and pulse. The ordinary dose of urotropin is 0.2–0.5 gm. (gr. iij.–viij.), and Nicolaier advises that 1.5 gm. (gr. xxiij.) a day should not be exceeded. It is best administered with plenty of water in small doses frequently repeated.

Loebisch has proposed the employment of urotropin as an intestinal disinfectant, its administration in intestinal putrefaction being more promptly followed by absence of indican in the urine than is the case with salol and other much-used drugs. It is absorbed very rapidly, however, and practically all of it is excreted in the urine; so it hardly seems probable that appreciable quantities of it can act in the intestine. Joseph Eastman thinks it may prove of value in puerperal sepsis. *W. A. Bastedo.*

URTICARIA.—Urticaria is an affection of the skin of which the salient characteristic is the occurrence of peculiar lesions called wheals. The description of wheals therefore covers in large part the objective symptoms of urticaria.

A wheal is a circumscribed elevation of the skin due to œdema of the corium. A typical wheal is the lesion produced in the average individual by the bite of a mosquito or flea. The typical wheal is slightly elevated, sharply circumscribed, with a flat or rounded surface, and of irregular or oval outline. The centre is usually pale and bloodless, but around this pale elevated centre there is an erythematous halo. The pressure of the edge of the finger nail on a wheal causes a slowly disappearing pitting, as in other œdema. The development of a wheal takes place suddenly. The first evidence of it is a rapidly appearing erythematous spot which itches, and upon which there suddenly develops a flat, œdematous swelling. The whole evolution of the lesion may occur in a few seconds. The duration is usually short, from a few minutes to an hour or two, though occasionally the le-

sions last for one or two days, and at times they persist for a week or more. Upon the disappearance of a wheal, if there has been no traumatism from scratching, no trace is usually left. At times, however, there is slight pigmentation, and if, as frequently happens, there has been vigorous scratching, inflamed papules or excoriations remain as a result of the traumatism.

As would be expected of so capricious a lesion there are numerous variations upon this typical wheal, and various subvarieties of urticaria are described according to the predominating form of wheals which characterize them. Wheals vary in size most widely. Typical wheals are usually from the size of a split pea to that of a finger nail. At times they are not larger than small papules and indeed are almost indistinguishable from ordinary inflammatory papules. They are frequently of the size of a twenty-five-cent piece, and in extreme cases are much larger. The writer has seen a wheal of which the elevation was not greater than a quarter of an inch, which extended around the chest from the median line in front to the median line at the back, and from the line of the nipple above to below the border of the ribs (*urticaria gigans*). Their shape is equally uncertain. Usually of more or less oval outline, they at times assume most irregular shapes, and, in persons whose skins are particularly susceptible to the production of wheals, they may be produced of any shape (*urticaria factitia*). In color they vary from inflammatory red to waxy white. If the œdema is intense enough to press out the blood from the capillaries, they show as a pale waxy centre with a narrow red periphery. Where the œdema is not so intense, or where the looseness of the tissues prevents extreme pressure from the œdema, the lesions are red in evidence of the hyperæmia. Occurring in tissues like the prepuce and eyelids, which are lax and offer, therefore, little resistance to the outpouring of serum, the lesions often form tumor-like œdematous swellings that closely resemble an inflammatory process in the same tissues (*urticaria tuberosa*). They are differentiated by their sudden appearance and equally sudden subsidence and the entire absence of pain. Very rarely the pressure of the extravasated fluid in the skin is sufficient to cause uplifting of the epidermis, so that the wheal is capped with a vesicle or bulla (*urticaria bullosa*). In still rarer instances the extravasation of serum is accompanied by enough red blood corpuscles to make the contents of these vesicles or bullæ hemorrhagic (*urticaria hæmorrhagica*).

In an acute attack of urticaria there is a sudden outbreak of wheals preceded and accompanied by more or less itching. There may be only a few lesions, or they may be innumerable. They occur on any part of the body, without symmetry and without any regularity of distribution. The acute attacks are often introduced by a transient systemic disturbance, with evidences of acute gastro-intestinal irritation. The temperature rises sharply three or four degrees, there are a rapid pulse, furred tongue, nausea and vomiting, and more or less prostration. At times evidences of a gastric crisis seem to indicate the involvement of the stomach in this peculiar angioneurotic process. The lesions themselves are characterized by intense itching. This itching may occur not only in the wheals themselves, but often at points where no wheals are present. The itching usually precedes for a few minutes the appearance of the wheals, and it persists during their continuance. It is somewhat paroxysmal in character, varying in intensity, without corresponding variation in the lesions. The itching varies in different cases and in different individuals, and according to the site of the lesions. Lesions in loose tissue may be accompanied by no itching whatever, while those occurring in dense thick skin and where the sensory nerve supply is richest, as on the hands and feet, are characterized by the most intense itching.

The course of an acute attack of urticaria usually extends over a few hours or at most a day or two, the disease passing away after the appearance of several crops of evanescent lesions. At times, however, the disease persists for weeks and months in successive outbreaks of the eruption, and in such cases is characterized as urticaria chronica, the term referring to the persistence of the process as a whole rather than to any peculiarity of the individual attacks. On the other hand, urticaria is persistent at times not only from the occurrence of repeated outbreaks of the eruption, but because the lesions lose their evanescent character and persist for days or weeks (*urticaria perstans*).

The *urticaria papulosa* of children, described by English dermatologists, is the best type of persistent urticaria. The characteristics of this form are the persistence of the lesions and the fact that the true urticarial wheals are followed by inflammatory papules which may persist for several weeks. It is readily seen that the occurrence of successive crops of wheals, which themselves persist for days or weeks and are followed by inflammatory papules which persist even longer, will produce an exaggerated picture of the urticarial skin. In such cases, as a result of scratching, we have inflamed papules, infected excoriations and more or less dermatitis, that results in thickening and induration of the skin. These cases in their most extreme type are strikingly similar to Hebra's prurigo. It is indeed not unlikely that they pass at times into true prurigo.

It is not an infrequent experience to see the vaso-motor mechanism so delicate that wheals may be produced at will by friction or other slight traumatism (urticaria factitia). In cases of acute urticaria this phenomenon is usual. In certain individuals this vaso-motor instability is inherent, so that factitious wheals may be produced at any time by slight traumatism, as drawing a line on the skin with a little force with a blunt stick or a finger nail. In such cases it is of course possible to produce wheals of any shape, so that names and elaborate designs may easily be written in wheals upon the skin (*dermographism*).

Urticaria tuberosa, urticaria bullosa, and urticaria hæmorrhagica have been referred to above. The peculiarities of the lesions of urticaria tuberosa depend almost solely upon their location at sites where the skin is very loose, and the lesions deserve no especial mention except to call attention to their somewhat confusing appearance at times. The lesions of urticaria bullosa and urticaria hæmorrhagica are usually seen in run-down individuals living under unfavorable conditions. Urticaria bullosa occurs most frequently in children. Urticaria hæmorrhagica is frequently associated with other evidences of hemorrhagic tendency, as hemorrhage from the mucous membranes, from the bowels and from the genito-urinary tract, and it is an evidence of a more profound systemic disturbance than usually exists in urticaria. Both of these forms of urticaria are rare.

The term giant urticaria is applied to urticaria which is characterized by the development of one or more wheals of very large size. They may be typical wheals, but most frequently they are rapidly developing œdematous swellings of pinkish color that bear a very striking objective similarity to an acute cellulitis. Such swellings at times present very slight if any resemblance to an urticarial wheal. They occur most frequently about the face and extremities, and often form tense, angry-looking swellings that for the time cause alarming distortion. Frequent sites of these lesions are the eyelid, the cheek, the nose, the lips, and the ear, and on such parts they may cause the most grotesque deformity. The larynx is not an uncommon site for their development, and their occurrence in that location may be the cause of distressing dyspnœa. Very rarely has it been found necessary to perform tracheotomy in such cases. Usually these large lesions occur singly, but they may occur in successive outbreaks or several large lesions may occur at one time. These lesions, like other urticarial wheals, develop rapidly, usually in the course of a few minutes, and after persisting for a shorter or longer time as rapidly subside. They are painless, usually unaccompanied by itching, and, unless they interfere with some important function through their size, are the source of little discomfort. There may be slight constitutional